

10/645,746

=> d his

(FILE 'HOME' ENTERED AT 09:22:04 ON 25 MAY 2007)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 09:30:52 ON 25 MAY 2007

L1 183 S "RDE-1"  
L2 48776 S RANI OR (RNA (W) INTERFERENCE)  
L3 131 S L1 AND L2  
L4 8397838 S CLON? OR EXPRESS? OR RECOMBINANT  
L5 69 S L3 AND L4  
L6 36 DUP REM L5 (33 DUPLICATES REMOVED)  
E MELLO G C/AU  
L7 6 S E3  
E FIRE A/AU  
L8 300 S E3  
E TABARA H/AU  
L9 172 S E3-E5  
E GRISHOK A/AU  
L10 67 S E3-E5  
L11 512 S L7 OR L8 OR L9 OR L10  
L12 46 S L1 AND L11  
L13 13 DUP REM L12 (33 DUPLICATES REMOVED)

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NEWS 3 JAN 16 CA/CAPLUS Company Name Thesaurus enhanced and reloaded  
NEWS 4 JAN 16 IPC version 2007.01 thesaurus available on STN  
NEWS 5 JAN 16 WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data  
NEWS 6 JAN 22 CA/CAPLUS updated with revised CAS roles  
NEWS 7 JAN 22 CA/CAPLUS enhanced with patent applications from India  
NEWS 8 JAN 29 PHAR reloaded with new search and display fields  
NEWS 9 JAN 29 CAS Registry Number crossover limit increased to 300,000 in  
multiple databases  
NEWS 10 FEB 15 PATDPASPC enhanced with Drug Approval numbers  
NEWS 11 FEB 15 RUSSIAPAT enhanced with pre-1994 records  
NEWS 12 FEB 23 KOREAPAT enhanced with IPC 8 features and functionality  
NEWS 13 FEB 26 MEDLINE reloaded with enhancements  
NEWS 14 FEB 26 EMBASE enhanced with Clinical Trial Number field  
NEWS 15 FEB 26 TOXCENTER enhanced with reloaded MEDLINE  
NEWS 16 FEB 26 IFICDB/IFIPAT/IFIUDB reloaded with enhancements  
NEWS 17 FEB 26 CAS Registry Number crossover limit increased from 10,000  
to 300,000 in multiple databases  
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NEWS 19 MAR 16 CASREACT coverage extended  
NEWS 20 MAR 20 MARPAT now updated daily  
NEWS 21 MAR 22 LWPI reloaded  
NEWS 22 MAR 30 RDISCLOSURE reloaded with enhancements  
NEWS 23 APR 02 JICST-EPLUS removed from database clusters and STN  
NEWS 24 APR 30 GENBANK reloaded and enhanced with Genome Project ID field  
NEWS 25 APR 30 CHEMCATS enhanced with 1.2 million new records  
NEWS 26 APR 30 CA/CAPLUS enhanced with 1870-1889 U.S. patent records  
NEWS 27 APR 30 INPADOC replaced by INPADOCDB on STN  
NEWS 28 MAY 01 New CAS web site launched  
NEWS 29 MAY 08 CA/CAPLUS Indian patent publication number format defined  
NEWS 30 MAY 14 RDISCLOSURE on STN Easy enhanced with new search and display  
fields  
NEWS 31 MAY 21 BIOSIS reloaded and enhanced with archival data  
NEWS 32 MAY 21 TOXCENTER enhanced with BIOSIS reload  
NEWS 33 MAY 21 CA/CAPLUS enhanced with additional kind codes for German  
patents  
NEWS 34 MAY 22 CA/CAPLUS enhanced with IPC reclassification in Japanese  
patents  
  
NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT  
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.  
  
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FILE 'LIFESCI' ENTERED AT 09:30:52 ON 25 MAY 2007

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=> s "RDE-1"

L1 183 "RDE-1"

=> s RANi or (RNA (w) interference)

L2 48776 RANI OR (RNA (W) INTERFERENCE)

=> s l1 and l2

L3 131 L1 AND L2

=> s clon? or express? or recombinant

L4 8397838 CLON? OR EXPRESS? OR RECOMBINANT

=> s 13 and 14  
L5 69 L3 AND L4

=> dup rem 15  
PROCESSING COMPLETED FOR L5  
L6 36 DUP REM L5 (33 DUPLICATES REMOVED)

=> d 1-36 ibib ab

L6 ANSWER 1 OF 36 MEDLINE on STN  
ACCESSION NUMBER: 2007144659 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 17344882  
TITLE: RNA interference has second helpings.  
AUTHOR: Miska Eric A; Ahringer Julie  
SOURCE: Nature biotechnology, (2007 Mar) Vol. 25, No. 3, pp. 302-3.  
Journal code: 9604648. ISSN: 1087-0156.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: News Announcement  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200705  
ENTRY DATE: Entered STN: 9 Mar 2007  
Last Updated on STN: 2 May 2007  
Entered Medline: 1 May 2007

L6 ANSWER 2 OF 36 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2007022734 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 17158288  
TITLE: Secondary siRNAs result from unprimed RNA synthesis and  
form a distinct class.  
AUTHOR: Sijen Titia; Steiner Florian A; Thijssen Karen L; Plasterk  
Ronald H A  
CORPORATE SOURCE: Hubrecht Laboratory (NIOB-KNAW), Uppsalalaan 8, 3584 CT,  
the Netherlands.  
SOURCE: Science (New York, N.Y.), (2007 Jan 12) Vol. 315, No. 5809,  
pp. 244-7. Electronic Publication: 2006-12-07.  
Journal code: 0404511. E-ISSN: 1095-9203.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200701  
ENTRY DATE: Entered STN: 13 Jan 2007  
Last Updated on STN: 27 Jan 2007  
Entered Medline: 26 Jan 2007

AB In *Caenorhabditis elegans*, an effective RNA interference  
(RNAi) response requires the production of secondary short interfering  
RNAs (siRNAs) by RNA-directed RNA polymerases (RdRPs). We cloned  
secondary siRNAs from transgenic *C. elegans* lines expressing a  
single 22-nucleotide primary siRNA. Several secondary siRNAs start a few  
nucleotides downstream of the primary siRNA, indicating that non-RISC  
(RNA-induced silencing complex)-cleaved mRNAs are substrates for secondary  
siRNA production. In lines expressing primary siRNAs with  
single-nucleotide mismatches, secondary siRNAs do not carry the mismatch  
but contain the nucleotide complementary to the mRNA. We infer that RdRPs  
perform unprimed RNA synthesis. Secondary siRNAs are only of antisense  
polarity, carry 5' di- or triphosphates, and are only in the minority  
associated with RDE-1, the RNAi-specific Argonaute  
protein. Therefore, secondary siRNAs represent a distinct class of small  
RNAs. Their biogenesis depends on RdRPs, and we propose that each  
secondary siRNA is an individual RdRP product.

L6 ANSWER 3 OF 36 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2007:89927 BIOSIS  
DOCUMENT NUMBER: PREV200700084440  
TITLE: RNA interference: Big applause for  
silencing in Stockholm.  
AUTHOR(S): Zamore, Phillip D. [Reprint Author]  
CORPORATE SOURCE: Univ Massachusetts, Sch Med, Dept Mol Pharmacol and  
Biochem, Worcester, MA 01605 USA  
phillip.zamore@umassmed.edu  
SOURCE: Cell, (DEC 15 2006) Vol. 127, No. 6, pp. 1083-1086.  
CODEN: CELLB5. ISSN: 0092-8674.  
DOCUMENT TYPE: Article  
General Review; (Literature Review)  
LANGUAGE: English  
ENTRY DATE: Entered STN: 31 Jan 2007  
Last Updated on STN: 31 Jan 2007  
AB Eight years ago, Craig Mello, Andrew Fire, and their coworkers provided  
the first demonstration that double-stranded RNA (dsRNA) triggers the  
gene-silencing technique that we now call RNA  
interference (RNAi). For this landmark discovery, Mello and Fire  
are honored with this year's Nobel Prize in Physiology or Medicine.

L6 ANSWER 4 OF 36 MEDLINE on STN  
ACCESSION NUMBER: 2006672552 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 17110334  
TITLE: Analysis of the C. elegans Argonaute family reveals that  
distinct Argonautes act sequentially during RNAi.  
AUTHOR: Yigit Erbay; Batista Pedro J; Bei Yanxia; Pang Ka Ming;  
Chen Chun-Chieh G; Tolia Niraj H; Joshua-Tor Leemor; Mitani  
Shohei; Simard Martin J; Mello Craig C  
CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts  
Medical School, Worcester, MA 01605, USA.  
CONTRACT NUMBER: GM58800 (NIGMS)  
SOURCE: Cell, (2006 Nov 17) Vol. 127, No. 4, pp. 747-57.  
Journal code: 0413066. ISSN: 0092-8674.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200612  
ENTRY DATE: Entered STN: 21 Nov 2006  
Last Updated on STN: 23 Dec 2006  
Entered Medline: 22 Dec 2006

AB Argonaute (AGO) proteins interact with small RNAs to mediate gene  
silencing. C. elegans contains 27 AGO genes, raising the question of what  
roles these genes play in RNAi and related gene-silencing pathways. Here  
we describe 31 deletion alleles representing all of the previously  
uncharacterized AGO genes. Analysis of single- and multiple-AGO mutant  
strains reveals functions in several pathways, including (1) chromosome  
segregation, (2) fertility, and (3) at least two separate steps in the  
RNAi pathway. We show that RDE-1 interacts with  
trigger-derived sense and antisense RNAs to initiate RNAi, while several  
other AGO proteins interact with amplified siRNAs to mediate downstream  
silencing. Overexpression of downstream AGOs enhances silencing,  
suggesting that these proteins are limiting for RNAi. Interestingly,  
these AGO proteins lack key residues required for mRNA cleavage. Our  
findings support a two-step model for RNAi, in which functionally and  
structurally distinct AGOs act sequentially to direct gene silencing.

L6 ANSWER 5 OF 36 MEDLINE on STN DUPLICATE 2  
ACCESSION NUMBER: 2005441202 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 16107851  
TITLE: Animal virus replication and RNAi-mediated antiviral

silencing in *Caenorhabditis elegans*.  
 AUTHOR: Lu R; Maduro M; Li F; Li H W; Broitman-Maduro G; Li W X; Ding S W  
 CORPORATE SOURCE: Institute for Integrative Genome Biology and Department of Plant Pathology, University of California, Riverside, California 92521, USA.  
 CONTRACT NUMBER: R01 AI052447-03 (NIAID)  
 SOURCE: Nature, (2005 Aug 18) Vol. 436, No. 7053, pp. 1040-3. Journal code: 0410462. E-ISSN: 1476-4687.  
 PUB. COUNTRY: England: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, N.I.H., EXTRAMURAL)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)  
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200509  
 ENTRY DATE: Entered STN: 19 Aug 2005  
 Last Updated on STN: 8 Sep 2005  
 Entered Medline: 7 Sep 2005

AB The worm *Caenorhabditis elegans* is a model system for studying many aspects of biology, including host responses to bacterial pathogens, but it is not known to support replication of any virus. Plants and insects encode multiple Dicer enzymes that recognize distinct precursors of small RNAs and may act cooperatively. However, it is not known whether the single Dicer of worms and mammals is able to initiate the small RNA-guided RNA interference (RNAi) antiviral immunity as occurs in plants and insects. Here we show complete replication of the Flock house virus (FHV) bipartite, plus-strand RNA genome in *C. elegans*. We show that FHV replication in *C. elegans* triggers potent antiviral silencing that requires RDE-1, an Argonaute protein essential for RNAi mediated by small interfering RNAs (siRNAs) but not by microRNAs. This immunity system is capable of rapid virus clearance in the absence of FHV B2 protein, which acts as a broad-spectrum RNAi inhibitor upstream of *rde-1* by targeting the siRNA precursor. This work establishes a *C. elegans* model for genetic studies of animal virus-host interactions and indicates that mammals might use a siRNA pathway as an antiviral response.

L6 ANSWER 6 OF 36 MEDLINE on STN DUPLICATE 3  
 ACCESSION NUMBER: 2005137829 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 15741313  
 TITLE: Transcriptional silencing of a transgene by RNAi in the soma of *C. elegans*.  
 AUTHOR: Grishok Alla; Sinskey Jina L; Sharp Phillip A  
 CORPORATE SOURCE: Center for Cancer Research, McGovern Institute, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA.  
 CONTRACT NUMBER: P01-CA42063 (NCI)  
 P30-CA 14051 (NCI)  
 R37-GM34277 (NIGMS)  
 SOURCE: Genes & development, (2005 Mar 15) Vol. 19, No. 6, pp. 683-96. Electronic Publication: 2005-03-01. Journal code: 8711660. ISSN: 0890-9369.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: (COMPARATIVE STUDY)  
 Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200504  
 ENTRY DATE: Entered STN: 17 Mar 2005

Last Updated on STN: 19 Apr 2005

Entered Medline: 18 Apr 2005

AB The silencing of transgene expression at the level of transcription in the soma of *Caenorhabditis elegans* through an RNAi-dependent pathway has not been previously characterized. Most gene silencing due to RNAi in *C. elegans* occurs at the post-transcriptional level. We observed transcriptional silencing when worms containing the *elt-2::gfp/LacZ* transgene were fed RNA produced from the commonly used L4440 vector. The transgene and the vector share plasmid backbone sequences. This transgene silencing depends on multiple RNAi pathway genes, including *dcr-1*, *rde-1*, *rde-4*, and *rrf-1*. Unlike post-transcriptional gene silencing in worms, *elt-2::gfp/LacZ* silencing is dependent on the PAZ-PIWI protein *Alg-1* and on the HP1 homolog *Hpl-2*. The latter is a chromatin silencing factor, and expression of the transgene is inhibited at the level of intron-containing precursor mRNA. This inhibition is accompanied by a decrease in the acetylation of histones associated with the transgene. This transcriptional silencing in the soma can be distinguished from transgene silencing in the germline by its inability to be transmitted across generations and its dependence on the *rde-1* gene. We therefore define this type of silencing as RNAi-induced Transcriptional Gene Silencing (RNAi-TGS). Additional chromatin-modifying components affecting RNAi-TGS were identified in a candidate RNAi screen.

L6 ANSWER 7 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:229753 SCISEARCH

THE GENUINE ARTICLE: 901FC

TITLE: A member of the polymerase beta nucleotidyltransferase superfamily is required for RNA interference in *C. elegans*

AUTHOR: Chen C C G; Simard M J; Tabara H; Brownell D R; McCollough J A; Mello C C (Reprint)

CORPORATE SOURCE: Univ Massachusetts, Sch Med, Program Mol Med, Worcester, MA 01605 USA (Reprint); Univ Massachusetts, Sch Med, Howard Hughes Med Inst, Worcester, MA 01605 USA; Kyoto Univ, HMRO, Grad Sch Med, Kyoto 6068501, Japan  
craig.mello@umassmed.edu

COUNTRY OF AUTHOR: USA; Japan

SOURCE: CURRENT BIOLOGY, (22 FEB 2005) Vol. 15, No. 4, pp. 378-383

ISSN: 0960-9822.

PUBLISHER: CELL PRESS, 1100 MASSACHUSETTS AVE, CAMBRIDGE, MA 02138 USA.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 20

ENTRY DATE: Entered STN: 10 Mar 2005

Last Updated on STN: 10 Mar 2005

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB RNA interference (RNAi) is an ancient, highly conserved mechanism in which small RNA molecules (siRNAs) guide the sequence-specific silencing of gene expression [1]. Several silencing machinery protein components have been identified, including helicases, RNase-related proteins, double- and singlestranded RNA binding proteins, and RNA-dependent RNA polymerase-related proteins [2]. Work on these factors has led to the revelation that RNAi mechanisms intersect with cellular pathways required for development and fertility [3, 4]. Despite rapid progress in understanding key steps in the RNAi pathway, it is clear that many factors required for both RNAi and related developmental mechanisms have not yet been identified. Here, we report the characterization of the *C. elegans* gene *rde-3*. Genetic analysis of presumptive null alleles indicates that *rde-3* is required for siRNA accumulation and for efficient RNAi in all tissues, and it is essential

for fertility and viability at high temperatures. RDE-3 contains conserved domains found in the polymerase beta nucleotidyltransferase superfamily, which includes conventional poly(A) polymerases, 2'-5' oligoadenylate synthetase (OAS), and yeast Trf4p [5]. These findings implicate a new enzymatic modality in RNAi and suggest possible models for the role of RDE-3 in the RNAi mechanism.

L6 ANSWER 8 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN  
ACCESSION NUMBER: 2005:659496 SCISEARCH  
THE GENUINE ARTICLE: 939JA  
TITLE: Molecular characterization of Entamoeba histolytica RNase III and AGO2, two RNA interference hallmark proteins  
AUTHOR: Abed M; Ankri S (Reprint)  
CORPORATE SOURCE: Technion Israel Inst Technol, Bruce Rappaport Fac Med, Dept Mol Microbiol, POB 9649, IL-31096 Haifa, Israel (Reprint); Technion Israel Inst Technol, Bruce Rappaport Fac Med, Dept Mol Microbiol, IL-31096 Haifa, Israel sankri@tx.technion.ac.il  
COUNTRY OF AUTHOR: Israel  
SOURCE: EXPERIMENTAL PARASITOLOGY, (JUL 2005) Vol. 110, No. 3, pp. 265-269.  
ISSN: 0014-4894.  
PUBLISHER: ACADEMIC PRESS INC ELSEVIER SCIENCE, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA.  
DOCUMENT TYPE: Article; Journal  
LANGUAGE: English  
REFERENCE COUNT: 19  
ENTRY DATE: Entered STN: 8 Jul 2005  
Last Updated on STN: 8 Jul 2005

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Entamoeba histolytica, a protozoan parasite with variable DNA content and complex ploidity, has defied most efforts aimed at gene depletion using classical genetic methods. In this study, we identified and characterized two proteins involved in the RNA interference (RNAi) pathway, RNase III and AGO2. Our results strengthen the findings that an RNAi pathway does exist in this parasite. (c) 2005 Elsevier Inc. All rights reserved.

L6 ANSWER 9 OF 36 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN  
DUPLICATE 4  
ACCESSION NUMBER: 2004-12362 BIOTECHDS  
TITLE: Inhibiting RNAi response in cell, by contacting cell with dsRNA involved in RNAi response, and inhibiting RNAi response, useful for increasing lifespan or treating premature aging in a subject who has abnormal aging disorder; RNA interference response inhibition for use in disease therapy and gene therapy  
AUTHOR: KENYON C; DILLIN A; MURPHY C  
PATENT ASSIGNEE: UNIV CALIFORNIA  
PATENT INFO: WO 2004029215 8 Apr 2004  
APPLICATION INFO: WO 2003-US30531 26 Sep 2003  
PRIORITY INFO: US 2002-413794 26 Sep 2002; US 2002-413794 26 Sep 2002  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2004-305156 [28]

AB DERWENT ABSTRACT:  
NOVELTY - Inhibiting (M1) an RNAi response in a cell, involves contacting the cell with a dsRNA involved in the RNAi response, thus inhibiting an RNAi response in a cell.  
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) inhibiting (M2) an RNAi response in a subject, involves administering a dsRNA involved in the RNAi response to the subject, thus



inhibiting an RNAi response in a cell; (2) increasing (M3) lifespan or treating premature aging in a subject, involves carrying out (M2); and (3) altering (M4) lifespan regulation in a subject, involves contacting the organism with a dsRNA involved in the RNAi response, thus inhibiting an RNAi response in a cell.

**BIOTECHNOLOGY - Preferred Method:** In (M1), the dsRNA is a dicer (dcr-1) dsRNA, a rde-1 dsRNA, an smg-5 dsRNA, an ego-1 dsRNA, or a rde-4 dsRNA. The inhibition of the RNAi response in a cell modulates an age-associated parameter, expression of a lifespan associated gene chosen from cellular stress-response gene, an antimicrobial gene, a metabolic gene, a steroid or lipid-soluble hormone synthesis gene, a fatty acid desaturation gene or its homolog or ortholog. The inhibition of the RNAi response modulates the expression of a lifespan associated gene chosen from cytochrome P450, an estradiol-17-beta-dehydrogenase, a alcohol/short-chain dehydrogenase, an esterase, a UDP-glucuronosyltransferase, an aminopeptidase, a carboxypeptidase, an amino-oxidase, an aminoacylase, an oligopeptide transporter, metallothionein, a receptor guanylate cyclase, a mitochondrial superoxide dismutase, a catalase, lysozyme, saposin, vitellogenin, glutathione-S-transferase, heat-shock protein, heat-shock factor, an F-box/cullin/Skp protein, an isocitrate lyase, a malate synthase ASMTL, insulin, IFG1 or IFG2 or its homolog or ortholog. The dcr-1 is human dcr-1, or *C. elegans* dcr-1. The age-associated parameter is lifespan. The modulation is inhibition of aging. The homolog or ortholog is a human homolog or ortholog.

**ACTIVITY -** Dermatological; Vasotropic; Nootropic; Cytostatic.

**MECHANISM OF ACTION -** Inhibitor of RNAi response (claimed). The ability of dicer dsRNA to inhibit RNAi response in a cell was determined. To lower daf-2 activity during the larval stages only, wild-type animals were grown on bacteria expressing daf-2 dsRNA and then shifted to bacteria expressing dcr-1 dsRNA as day 1 adults. Control animals were grown during development on the RNAi bacteria containing the vector only and then shifted to dcr-1 RNAi bacteria as day 1 adults. Animals were grown at 25 degrees C. Daf-2 RNA was inactivated using daf-2 specific RNAi. The animals were removed from the environment RNAi stimulus (food bacteria expressing daf-2 dsRNA). The RNAi response continued to exert its effect during the adult stages and caused an increased lifespan. By shifting these animals to dcr-1 RNAi in early adulthood, increased lifespan was blocked, by blocking the existing RNAi response against daf-2. In the second experiment loss of mitochondrial electron transport activity during the early development stages caused an increased adult lifespan. In contrast to the daf-2 experiment, this increased lifespan could not be reduced if the animals were shifted to dcr-1 RNAi as adults.

**USE -** (M1) is useful for inhibiting an RNAi response in a cell. (M2) is useful for inhibiting an RNAi response in a subject which is a mammal, preferably an adult. The mammal is a non-diabetic, non-obese adult who is not at risk for or does not have a premature aging disorder. The mammal is a healthy adult. (M3) is useful for increasing lifespan or treating premature aging in a subject who has abnormal aging disorder such as Werner syndrome, Hutchinson-Guilford disease, Bloom's syndrome, Cockayne's syndrome, ataxia telangiectasia, and Down's syndrome (claimed).

**ADMINISTRATION -** The dcr-1 dsRNA is administered by parental, oral, inhalation, transdermal or rectal routes of administration. No specific dosage details are given.

**EXAMPLE -** Total RNA was extracted from approximately 20000 synchronized, sterile animals using trizol. Before harvest, animals were exposed to bacteria containing the RNAi vector or containing the daf-2 RNAi construct from the L1 until the L4 larval stage or from day 8 until day 10 of adulthood. Four mug of total RNA was used for one round of reverse transcription (RT) using oligo dT primers. Serial dilutions of the RT reaction (1:1-1:245) was used for PCR reaction using daf-2 specific primers. RNAi was directed to a non-overlapping 5' end of daf-2.

Serial dilutions of the RT reaction (1:1-1:2) was used for PCR reaction using daf-16 specific primers. RNAi was directed to a non-overlapping 5' end of daf-16. Four mul of a 50 mul PCR reaction was analyzed on agarose gels using ethidium bromide. Wild-type hermaphrodites were allowed to lay eggs onto the control RNAi bacteria or daf-2 RNAi bacteria at 20 degreesC. The eggs were then shifted to 27 degreesC and the presence of dauer larvae were scored 48 hours later when animals would normally be reproductive adults. Lifespan, reproduction and stress assays were conducted at 20 degreesC. The total number of progeny born to a single worm over time was measured. Briefly, worms hatched within a 1 hour period was collected and allowed to develop to the L4 stage. Once in the L4 stage, worms were individually placed onto separate plates. In all cases, at least 15 worms were used for each analysis. Worms were transferred to new plates every 12 hours and the resulting progeny were allowed to grow for two days until counted for progeny measurements. The % of total progeny was calculated for each time point by dividing the number of progeny produced on a time point by the total number of progeny produced over the course of the experiment. (70 pages)

L6 ANSWER 10 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:149012 SCISEARCH

THE GENUINE ARTICLE: 773AJ

TITLE: A conserved siRNA-degrading RNase negatively regulates RNA interference in C-elegans

AUTHOR: Kennedy S; Wang D; Ruvkun G (Reprint)

CORPORATE SOURCE: Harvard Univ, Massachusetts Gen Hosp, Sch Med, Dept Mol Biol, Boston, MA 02114 USA (Reprint); Harvard Univ, Sch Med, Dept Genet, Boston, MA 02114 USA

COUNTRY OF AUTHOR: USA

SOURCE: NATURE, (12 FEB 2004) Vol. 427, No. 6975, pp. 645-649. ISSN: 0028-0836.

PUBLISHER: NATURE PUBLISHING GROUP, MACMILLAN BUILDING, 4 CRINAN ST, LONDON N1 9XW, ENGLAND.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 21

ENTRY DATE: Entered STN: 20 Feb 2004

Last Updated on STN: 20 Feb 2004

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB In many organisms, introducing double-stranded RNA (dsRNA) causes the degradation of messenger RNA that is homologous to the trigger dsRNA-a process known as RNA interference. The dsRNA is cleaved into short interfering RNAs (siRNAs), which hybridize to homologous mRNAs and induce their degradation(1). dsRNAs vary in their ability to trigger RNA interference: many mRNA-targeting dsRNAs show weak phenotypes, and nearly all mRNAs of the *Caenorhabditis elegans* nervous system are refractory to RNA interference(2-4). *C. elegans* eri-1 was identified in a genetic screen for mutants with enhanced sensitivity to dsRNAs. Here we show that eri-1 encodes an evolutionarily conserved protein with domains homologous to nucleic-acid-binding and exonuclease proteins. After exposure to dsRNA or siRNAs, animals with eri-1 mutations accumulate more siRNAs than do wild-type animals. *C. elegans* ERI-1 and its human orthologue degrade siRNAs in vitro. In the nematode worm, ERI-1 is predominantly cytoplasmic and is expressed most highly in the gonad and a subset of neurons, suggesting that ERI-1 siRNase activity suppresses RNA interference more intensely in these tissues. Thus, ERI-1 is a negative regulator that may normally function to limit the duration, cell-type specificity or endogenous functions of RNA interference.

L6 ANSWER 11 OF 36 MEDLINE on STN

ACCESSION NUMBER: 2004352241 MEDLINE

DUPLICATE 5

DOCUMENT NUMBER: PubMed ID: 15255192  
TITLE: Metalloproteases with EGF, CUB, and thrombospondin-1 domains function in molting of *Caenorhabditis elegans*.  
AUTHOR: Suzuki Mami; Sagoh Noriko; Iwasaki Hideki; Inoue Hideshi; Takahashi Kenji  
CORPORATE SOURCE: Laboratory of Molecular Biochemistry, School of Life Science, Tokyo University of Pharmacy and Life Science, 1432-1 Horinouchi, Hachioji, Tokyo 192-0392, Japan.  
SOURCE: Biological chemistry, (2004 Jun) Vol. 385, No. 6, pp. 565-8.  
Journal code: 9700112. ISSN: 1431-6730.  
PUB. COUNTRY: Germany: Germany, Federal Republic of  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200501  
ENTRY DATE: Entered STN: 17 Jul 2004  
Last Updated on STN: 28 Jan 2005  
Entered Medline: 27 Jan 2005

AB Functional analysis using RNAi was performed on eleven genes for metalloproteases of the M12A family in *Caenorhabditis elegans* and the interference of the C17G1.6 gene (nas-37) was found to cause incomplete molting. The RNAi of the C26C6.3 gene (nas-36) also caused a similar molting defect but not so severely as that of the nas-37 gene. Both the genes encode an astacin-like metalloprotease with an epidermal growth factor (EGF)-like domain, a CUB domain, and a thrombospondin-1 domain, in this order. The promoter-driven green fluorescent protein (GFP) expression analysis suggested that they are expressed in hypodermal cells throughout the larval stages and in the vulva of adult animals. In the genetic background of *rde-1(ne219)*, where RNAi does not work, the molting defect caused by the nas-37 interference was observed when the transgenic wild-type *rde-1* gene was expressed under the control of the *dpy-7* promoter, known to be active in the hypodermal cells, but not under the control of the *myo-3* promoter, active in the muscular cells. Therefore these proteases are thought to be secreted by the hypodermal cells and to participate in shedding of old cuticles.

L6 ANSWER 12 OF 36 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:240580 HCAPLUS  
DOCUMENT NUMBER: 141:49068  
TITLE: RNA interference: a practical approach  
AUTHOR(S): Duxbury, Mark S.; Whang, Edward E.  
CORPORATE SOURCE: Brigham and Women's Hospital, Department of Surgery, Harvard Medical School, Boston, MA, 02115, USA  
SOURCE: Journal of Surgical Research (2004), 117(2), 339-344  
CODEN: JSGRA2; ISSN: 0022-4804  
PUBLISHER: Elsevier Science  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

AB A review. Few new mol. biol. techniques have advanced to find practical application as rapidly as RNA interference (RNAi). RNAi denotes the highly specific posttranslational silencing of gene expression that occurs in response to the introduction of double-stranded RNA into a cell. The purpose of this review is to present practical guidelines for designing and executing RNAi expts. We summarize the mechanisms underlying RNAi in mammalian cells and focus on practical advice for investigators conducting RNAi expts. We suggest criteria to help select a suitable target gene sequence, define the structural characteristics of effective siRNAs, discuss transfection strategies, and describe exptl. design, including important control methods. RNAi represents a powerful tool for determining the functions of specific genes.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 36 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN  
DUPLICATE 6

ACCESSION NUMBER: 2004-00966 BIOTECHDS

TITLE: Novel embryonic stem cell having increased RNA  
interference effect and obtained by genetically  
manipulating embryonic stem cells, useful for analysis of  
gene function in organisms;  
functional genomics study involving use of transfected  
stem cell and transgenic animal model

PATENT ASSIGNEE: GENCOM KK

PATENT INFO: JP 2003144141 20 May 2003

APPLICATION INFO: JP 2001-348705 14 Nov 2001

PRIORITY INFO: JP 2001-348705 14 Nov 2001; JP 2001-348705 14 Nov 2001

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

OTHER SOURCE: WPI: 2003-818155 [77]

AB DERWENT ABSTRACT:

NOVELTY - Embryonic stem cell (I) having increased RNA  
interference (RNAi) effect obtained by genetically manipulating  
an embryonic stem cell, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a  
non-human mammal and its off spring derived from (I) or its part.

BIOTECHNOLOGY - Preferred Stem cell: (I) is obtained by introducing  
a RNAi related gene to an embryonic stem cell. The RNAi related gene is a  
gene which codes a factor associated with the formation of a sequence  
specific intermediate, a gene which codes a factor associated with target  
gene suppression, a gene which codes a RNA dependent RNA polymerase or a  
gene which codes a helicase. The RNAi related gene is preferably Nematode  
rde-1 or rde-4 gene, fungi qde-2 gene, Arabidopsis  
ago-1 gene, a dicer gene or its homolog gene which codes the protein of a  
PAZ/Piwi family etc., nematode Mut-7 gene, nematode rde-2, fungi qde-1  
gene, nematode ego-1 gene, Arabidopsis sgs 2/sde 1 gene, fungi qde-3  
gene, nematode smg-2 gene, Chlamydomonas mut 6 gene or Arabidopsis sde 3  
gene, more preferably nematode rde-1 gene or Mut-7  
gene. (I) is obtained by introducing a expression vector  
containing a RNAi related gene which can be expressed within a  
host cell, into an embryonic stem cell. (I) further comprises a  
recombinant gene (II) which contains a inverse repeat sequence of  
a target gene that can be expressed in a mammalian cell. (II)  
is present downstream of a promoter sequence functional in mammalian  
cell. (II) contains an enhancer sequence in the upstream of the promoter  
sequence, and further contains an insulator sequence or its fragment.  
(II) contains a poly A addition signal sequence in the downstream of the  
inverse repeat sequence of a target gene e.g., exogenous reporter protein  
or a gene encoding a variant protein. Preferably the exogenous reporter  
protein is enhanced green fluorescent protein (EGFP). Embryonic stem cell  
has an accession-number FERM P-18574 or P-18575. Preferred Mammal: The  
non-human mammal or its offspring is chosen from mouse, rat, hamster,  
guinea pig, rabbit dog, cat, horse, cow, sheep, pig, goat, and monkey.

USE - (I) is useful for analysis of gene function.

ADVANTAGE - A gene can be suppressed reliably. Related genes can be  
analyzed rapidly compared to the knock-out method.

EXAMPLE - A embryonic stem cell d2EGFP was established as follows.  
The target gene encoding enhanced green fluorescent protein (EGFP) was  
used to establish the stem cell d2EGFP. The d2EGFP expression  
vector used was pUC19 5', 3' INS24 OCE EGFP. The vector was further  
inserted with an insulation sequence, a cytomegalovirus (CMV) enhances  
sequence and an EF-1 alpha sequence inserted to the right side of the  
BamH I fragment and pd2EGFP 5' INS240 CE was obtained. pd2EGFP 5' INS240  
CE was digested using EcoR I and Bsa I and transfected into embryonic  
stem cell by electroporation method. pd2EGFP embryonic stem cell strain

colony was confirmed by the EGFP fluorescence detected using a fluorescence microscope. The embryonic stem cells were cultured by standard methods. Each embryonic stem cell proliferated on the feeder cell was peeled by trypsin-EDTA and cultured in an gelatin coated plate. Then it was transfected using pUC19 5' INS240 EGFP IR having EGFP dsRNA gene containing inverse repeat sequence JP2001046089. A control was built using the plasmid with HPRT (Hypoxanthine phosphoribosyl transferase) dsRNA expression gene (inverse repeat sequence gene). The fluorescence of the cells were analyzed by FACScan. The fluorescence reduction was compared with the control which does not contain the gene. The results showed that the fluorescent reduction of the cell raises 28% compared to the control. (17 pages)

L6 ANSWER 14 OF 36 HCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2003:417858 HCAPLUS  
 DOCUMENT NUMBER: 139:1986  
 TITLE: Facilitation of RNA interference  
 (RNAi) in mammalian cell using invertebrate  
 RNA-dependent RNA polymerase (RdRP) gene family  
 involved in RNAi  
 INVENTOR(S): Mello, Craig C.; Conte, Darryl, Jr.; Chen, Chun-Chieh  
 PATENT ASSIGNEE(S): University of Massachusetts, USA  
 SOURCE: PCT Int. Appl., 47 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003044168	A2	20030530	WO 2002-US36725	20021115
WO 2003044168	A9	20040506		
WO 2003044168	A3	20040826		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002360394	A1	20030610	AU 2002-360394	20021115
US 2003114409	A1	20030619	US 2002-295809	20021115
PRIORITY APPLN. INFO.:			US 2001-333811P	P 20011116
			US 2001-331672P	P 20011119
			WO 2002-US36725	W 20021115

AB The present invention features compns. and methods to induce or enhance RNA interference (RNAi) in cells, systems, and organisms using mols. that mediate RNAi in invertebrates such as Caenorhabditis elegans. The invention is based, in part, on the discovery that members of the C. elegans RNA-dependent RNA polymerase (RdRP) gene family, namely ego-1 and rrf-1 genes, are involved in, and can be essential for, RNAi. Thus, RdRP expression can be used to induce or enhance RNAi in cells, including mammalian cells. RdRP genes can be expressed in combination with one or more of the other genes of the RNAi system, such as Dicer, RDE-1, or RDE-4.

L6 ANSWER 15 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN  
 ACCESSION NUMBER: 2003:636265 SCISEARCH  
 THE GENUINE ARTICLE: 701CB

TITLE: Inducible systemic RNA silencing in *Caenorhabditis elegans*  
AUTHOR: Timmons L (Reprint); Tabara H; Mello C C; Fire A Z  
CORPORATE SOURCE: Univ Kansas, Dept Mol Biosci, Lawrence, KS 66045 USA  
(Reprint); Univ Tokushima, Tokushima 7708503, Japan; Univ  
Massachusetts, Sch Med, Howard Hughes Med Inst, Worcester,  
MA 01605 USA; Univ Massachusetts, Sch Med, Dept Cell Biol,  
Worcester, MA 01605 USA; Carnegie Inst Washington, Dept  
Embryol, Baltimore, MD 21210 USA  
COUNTRY OF AUTHOR: USA; Japan  
SOURCE: MOLECULAR BIOLOGY OF THE CELL, (JUL 2003) Vol. 14, No. 7,  
pp. 2972-2983.  
ISSN: 1059-1524.  
PUBLISHER: AMER SOC CELL BIOLOGY, 8120 WOODMONT AVE, STE 750,  
BETHESDA, MD 20814-2755 USA.  
DOCUMENT TYPE: Article; Journal  
LANGUAGE: English  
REFERENCE COUNT: 58  
ENTRY DATE: Entered STN: 8 Aug 2003  
Last Updated on STN: 8 Aug 2003

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Introduction of double-stranded RNA (dsRNA) can elicit a gene-specific RNA interference response in a variety of organisms and cell types. In many cases, this response has a systemic character in that silencing of gene expression is observed in cells distal from the site of dsRNA delivery. The molecular mechanisms underlying the mobile nature of RNA silencing are unknown. For example, although cellular entry of dsRNA is possible, cellular exit of dsRNA from normal animal cells has not been directly observed. We provide evidence that transgenic strains of *Caenorhabditis elegans* transcribing dsRNA from a tissue-specific promoter do not exhibit comprehensive systemic RNA interference phenotypes. In these same animals, modifications of environmental conditions can result in more robust systemic RNA silencing. Additionally, we find that genetic mutations can influence the systemic character of RNA silencing in *C. elegans* and can separate mechanisms underlying systemic RNA silencing into tissue-specific components. These data suggest that trafficking of RNA silencing signals in *C. elegans* is regulated by specific physiological and genetic factors.

L6 ANSWER 16 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN  
ACCESSION NUMBER: 2003:770070 SCISEARCH  
THE GENUINE ARTICLE: 720HL  
TITLE: Transport of dsRNA into cells by the transmembrane protein SID-1  
AUTHOR: Feinberg E H; Hunter C P (Reprint)  
CORPORATE SOURCE: Harvard Univ, Dept Mol & Cellular Biol, 16 Divin Ave, Cambridge, MA 02138 USA (Reprint); Harvard Univ, Dept Mol & Cellular Biol, Cambridge, MA 02138 USA  
COUNTRY OF AUTHOR: USA  
SOURCE: SCIENCE, (12 SEP 2003) Vol. 301, No. 5639, pp. 1545-1547.  
ISSN: 0036-8075.  
PUBLISHER: AMER ASSOC ADVANCEMENT SCIENCE, 1200 NEW YORK AVE, NW, WASHINGTON, DC 20005 USA.  
DOCUMENT TYPE: Article; Journal  
LANGUAGE: English  
REFERENCE COUNT: 21  
ENTRY DATE: Entered STN: 19 Sep 2003  
Last Updated on STN: 19 Sep 2003

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB RNA interference (RNAi) spreads systemically in plants and nematodes to silence gene expression distant from the site of initiation. We previously identified a gene, *sid-1*, essential for systemic but not cell-autonomous RNAi in *Caenorhabditis elegans*. Here, we demonstrate that SID-1 is a multispan transmembrane protein that

sensitizes *Drosophila* cells to soaking RNAi with a potency that is dependent on double-stranded RNA ( dsRNA) length. Further analyses revealed that SID-1 enables passive cellular uptake of dsRNA. These data indicate that systemic RNAi in *C. elegans* involves SID-1-mediated intercellular transport of dsRNA.

L6 ANSWER 17 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN  
 ACCESSION NUMBER: 2003:426753 SCISEARCH  
 THE GENUINE ARTICLE: 679CK  
 TITLE: Arabidopsis HEN1: A genetic link between endogenous miRNA controlling development and siRNA controlling transgene silencing and virus resistance  
 AUTHOR: Boutet S; Vazquez F; Liu J; Beclin C; Fagard M; Gratias A; Morel J B; Crete P; Chen X M; Vaucheret H (Reprint)  
 CORPORATE SOURCE: INRA, Biol Cellulaire Lab, F-78026 Versailles, France (Reprint); USTL, Lab Physiol Differentiat Vegetale, F-59650 Villeneuve Dascq, France; Rutgers State Univ, Waksman Inst, Piscataway, NJ 08854 USA  
 COUNTRY OF AUTHOR: France; USA  
 SOURCE: CURRENT BIOLOGY, (13 MAY 2003) Vol. 13, No. 10, pp. 843-848.  
 ISSN: 0960-9822.  
 PUBLISHER: CELL PRESS, 1100 MASSACHUSETTS AVE, CAMBRIDGE, MA 02138 USA.  
 DOCUMENT TYPE: Article; Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 30  
 ENTRY DATE: Entered STN: 9 Jun 2003  
 Last Updated on STN: 9 Jun 2003

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB In animals, double-stranded short interfering RNA (siRNA) and single-stranded microRNA (miRNA) regulate gene expression by targeting homologous mRNA for cleavage or by interfering with their translation, respectively [1-3]. siRNAs are processed from injected or transgene-derived, long, perfect double-stranded RNA (dsRNA), while miRNAs are processed from short, imperfect dsRNA precursors transcribed from endogenous intergenic regions [4-9]. In plants, both siRNAs and miRNAs activate cleavage of homologous RNA targets [10-12], but little is known about the genes controlling their production or action. The SGS2/SDE1 protein contributes to produce transgene siRNA [10], while DCL1 and HEN1 contribute to endogenous miRNA accumulation [8, 9]. Here, we show that: i) SGS2, SGS3 [13], AGO1 [14,15], and HEN1 contribute to produce transgene siRNA involved in sense post-transcriptional gene silencing (S-PTGS); ii) HEN1, but not SGS2, SGS3, or AGO1, contributes to the accumulation of the endogenous miR171 miRNA and to the cleavage of Scarecrow target mRNA by miR171 [11]; iii) SGS2, SGS3, AGO1, and HEN I contribute to resistance against cucumber mosaic virus [13, 16], but not to siRNA and IR-PTGS triggered by hairpin transgenes directly producing perfect dsRNA [16]; and iv) the actions of HEN1 in miRNA/development and siRNA/ S-PTGS can be uncoupled by single-point mutations at different positions in the protein.

L6 ANSWER 18 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN  
 ACCESSION NUMBER: 2003:682305 SCISEARCH  
 THE GENUINE ARTICLE: 706RN  
 TITLE: A gene encoding an RNase D exonuclease-like protein is required for post-transcriptional silencing in Arabidopsis  
 AUTHOR: Glazov E; Phillips K; Budziszewski G J; Meins F (Reprint); Levin J Z  
 CORPORATE SOURCE: Novartis Res Fdn, Friedrich Miescher Inst Biomed Res, Maulbeerstr 66, CH-4058 Basel, Switzerland (Reprint); Novartis Res Fdn, Friedrich Miescher Inst Biomed Res, CH-4058 Basel, Switzerland; Syngenta Biotechnol Inc, Res

Triangle Pk, NC 27709 USA  
COUNTRY OF AUTHOR: Switzerland; USA  
SOURCE: PLANT JOURNAL, (AUG 2003) Vol. 35, No. 3, pp. 342-349.  
ISSN: 0960-7412.  
PUBLISHER: BLACKWELL PUBLISHING LTD, 9600 GARSINGTON RD, OXFORD OX4  
2DG, OXON, ENGLAND.  
DOCUMENT TYPE: Article; Journal  
LANGUAGE: English  
REFERENCE COUNT: 43  
ENTRY DATE: Entered STN: 22 Aug 2003  
Last Updated on STN: 22 Aug 2003

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Post-transcriptional gene silencing (PTGS) and the closely related phenomenon RNA interference (RNAi) result from the initial endonucleolytic cleavage of target mRNAs, which are then presumed to be completely hydrolyzed by exoribonucleases. To date, no plant genes required for PTGS are known to encode exoribonucleases. The Arabidopsis Werner Syndrome-like exonuclease (WEX) gene encodes an RNase D domain most similar to that in human Werner Syndrome protein (WRN), but lacks the RecQ helicase domain. It is also related to Caenorhabditis elegans mut-7, which is essential for RNAi, PTGS, and transposon activity. We isolated a loss-of-function mutant, wex-1, that showed greatly reduced expression of WEX mRNA and early flowering. Although wex-1 did not affect expression of a robust marker for transcriptional gene silencing (TGS), PTGS of a green-fluorescent-protein (GFP) reporter gene was blocked in wex-1 and restored by ectopic expression of WEX, indicating that WEX is required for PTGS but not TGS. Thus, members of the RNase D protein family are required for PTGS in both plants and animals. Interestingly, WEX has been shown to interact with an Arabidopsis RecQ helicase, suggesting that these proteins might comprise a functional equivalent of WRN.

L6 ANSWER 19 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:1007849 SCISEARCH  
THE GENUINE ARTICLE: 744YQ  
TITLE: Transposon silencing in the Caenorhabditis elegans germ line by natural RNAi  
AUTHOR: Sijen T; Plasterk R H A (Reprint)  
CORPORATE SOURCE: Netherlands Inst Dev Biol, Hubrecht Lab, Uppsalalaan 8, NL-3584 CT Utrecht, Netherlands (Reprint); Netherlands Inst Dev Biol, Hubrecht Lab, NL-3584 CT Utrecht, Netherlands  
COUNTRY OF AUTHOR: Netherlands  
SOURCE: NATURE, (26 NOV 2003) Vol. 426, No. 6964, pp. 310-314.  
ISSN: 0028-0836.  
PUBLISHER: NATURE PUBLISHING GROUP, MACMILLAN BUILDING, 4 CRINAN ST, LONDON N1 9XW, ENGLAND.  
DOCUMENT TYPE: Article; Journal  
LANGUAGE: English  
REFERENCE COUNT: 30  
ENTRY DATE: Entered STN: 8 Dec 2003  
Last Updated on STN: 8 Dec 2003

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Transposable elements are stretches of DNA that can move and multiply within the genome of an organism. The Caenorhabditis elegans genome contains multiple Tc1 transposons that jump in somatic cells, but are silenced in the germ line(1-3). Many mutants that have lost this silencing have also lost the ability to execute RNA interference (RNAi) (2,3), a process whereby genes are suppressed by exposure to homologous double-stranded RNA (dsRNA). Here we show how RNAi causes transposon silencing in the nematode germ line. We find evidence for transposon-derived dsRNAs, in particular to the terminal inverted repeats, and show that these RNAs may derive from read-through



transcription of entire transposable elements. Small interfering RNAs of Tc1 were detected. When a germline-expressed reporter gene is fused to a stretch of Tc1 sequence, this transgene is silenced in a manner dependent on functional mutator genes (mut-7, mut-16 and pk732). These results indicate that RNAi surveillance is triggered by fortuitous read-through transcription of dispersed Tc1 copies, which can form dsRNA as a result of 'snap-back' of the terminal inverted repeats. RNAi mediated by this dsRNA silences transposase gene expression.

L6 ANSWER 20 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:173673 SCISEARCH

THE GENUINE ARTICLE: 645DF

TITLE: Posttranscriptional gene silencing is not compromised in the Arabidopsis CARPEL FACTORY (DICER-LIKE1) mutant, a homolog of dicer-1 from Drosophila

AUTHOR: Finnegan E J (Reprint); Margis R; Waterhouse P M

CORPORATE SOURCE: CSIRO, Plant Ind, POB 1600, Canberra, ACT 2601, Australia (Reprint); CSIRO, Plant Ind, Canberra, ACT 2601, Australia; Univ Fed Rio de Janeiro, Inst Chem, Dept Biochem, Rio De Janeiro, Brazil

COUNTRY OF AUTHOR: Australia; Brazil

SOURCE: CURRENT BIOLOGY, (4 FEB 2003) Vol. 13, No. 3, pp. 236-240. ISSN: 0960-9822.

PUBLISHER: CELL PRESS, 1100 MASSACHUSETTS AVE, CAMBRIDGE, MA 02138 USA.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 31

ENTRY DATE: Entered STN: 7 Mar 2003

Last Updated on STN: 7 Mar 2003

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Posttranscriptional silencing (PTGS) in plants, nematodes, Drosophila, and perhaps all eukaryotes; operates by sequence-specific degradation or translational inhibition of the target mRNA. These processes are mediated by duplexed RNA. In Drosophila and nematodes, double-stranded (ds)RNA or self-complementary RNA is processed into fragments of approximately 21 nt by Dicer-1 [1, 2]. These small interfering RNAs (siRNAs) serve as guides to target degradation of homologous single-stranded (ss)RNA [1, 3]. In some cases, the approximately 21 nt guide fragments derived from endogenous, imperfectly self-complementary RNAs cause translational inhibition of their target mRNAs, with which they have substantial, but not perfect sequence complementarity [4-6]. These small temporal RNAs (stRNAs) belong to a class of noncoding microRNAs (miRNAs), 20-24 nt in length, that are found in flies, plants, nematodes, and mammals [4, 6-12]. In nematodes, the Dicer-1 enzyme catalyzes the production of both siRNA and stRNA [2, 13-15]. Mutation of the Arabidopsis Dicer-1 homolog, CARPEL FACTORY (CAF), blocks miRNA production [1, 4, 16-18]. Here, we report that the same caf mutant does not block either PTGS or siRNA production induced by self-complementary hairpin RNA. This suggests either that this mutation only impairs miRNA formation or, more interestingly, that plants have two distinct dicer-like enzymes, one for miRNA and another for siRNA production.

L6 ANSWER 21 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:596077 SCISEARCH

THE GENUINE ARTICLE: 696HV

TITLE: Gene silencing in Caenorhabditis elegans by transitive RNA interference

AUTHOR: Alder M N; Dames S; Gaudet J; Mango S E (Reprint)

CORPORATE SOURCE: Univ Utah, Huntsmann Canc Inst, 200 Circle Hope, Salt Lake City, UT 84112 USA (Reprint); Univ Utah, Huntsmann Canc Inst, Salt Lake City, UT 84112 USA

COUNTRY OF AUTHOR: USA  
SOURCE: RNA-A PUBLICATION OF THE RNA SOCIETY, (JAN 2003) Vol. 9,  
No. 1, pp. 25-32.  
ISSN: 1355-8382.  
PUBLISHER: COLD SPRING HARBOR LAB PRESS, PUBLICATIONS DEPT, 500  
SUNNYSIDE BLVD, WOODBURY, NY 11797-2924 USA.  
DOCUMENT TYPE: Article; Journal  
LANGUAGE: English  
REFERENCE COUNT: 56  
ENTRY DATE: Entered STN: 25 Jul 2003  
Last Updated on STN: 25 Jul 2003

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB When a cell is exposed to double-stranded RNA (dsRNA), mRNA from the homologous gene is selectively degraded by a process called RNA interference (RNAi). Here, we provide evidence that dsRNA is amplified in *Caenorhabditis elegans* to ensure a robust RNAi response. Our data suggest a model in which mRNA targeted by RNAi functions as a template for 5' to 3' synthesis of new dsRNA (termed transitive RNAi). Strikingly, the effect is nonautonomous: dsRNA targeted to a gene expressed in one cell type can lead to transitive RNAi-mediated silencing of a second gene expressed in a distinct cell type. These data suggest dsRNA synthesized in vivo can mediate systemic RNAi.

L6 ANSWER 22 OF 36 MEDLINE on STN DUPLICATE 7  
ACCESSION NUMBER: 2002466218 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12225671  
TITLE: PPW-1, a PAZ/PIWI protein required for efficient germline RNAi, is defective in a natural isolate of *C. elegans*.  
AUTHOR: Tijsterman Marcel; Okihara Kristy L; Thijssen Karen; Plasterk Ronald H A  
CORPORATE SOURCE: Hubrecht Laboratory, Center for Biomedical Genetics, Uppsalaalaan 8, 3584 CT, Utrecht, The Netherlands.  
SOURCE: Current biology : CB, (2002 Sep 3) Vol. 12, No. 17, pp. 1535-40.  
Journal code: 9107782. ISSN: 0960-9822.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: (COMPARATIVE STUDY)  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200306  
ENTRY DATE: Entered STN: 13 Sep 2002  
Last Updated on STN: 17 Jun 2003  
Entered Medline: 16 Jun 2003

AB One of the remarkable aspects about RNA interference (RNAi) in *Caenorhabditis elegans* is that the trigger molecules, dsRNA, can be administered via the animal's food. We assayed whether this feature is a universal property of the species by testing numerous strains that have been isolated from different parts of the globe. We found that one isolate from Hawaii had a defect in RNAi that was specific to the germline and was a result of multiple mutations in a PAZ/PIWI domain-containing protein, which we named PPW-1. Deleting ppw-1 in the canonical *C. elegans* strain Bristol N2 makes it resistant to feeding of dsRNA directed against germline-expressed genes. PPW-1 belongs to the Argonaute family of proteins, which act in posttranscriptional gene silencing and development, and is homologous to the RNAi gene rde-1. Our data indicate that at least two members of this family are required for complete and effective RNAi in *C. elegans*.

L6 ANSWER 23 OF 36 MEDLINE on STN  
ACCESSION NUMBER: 2002364170 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12110183  
TITLE: The dsRNA binding protein RDE-4 interacts with RDE-1, DCR-1, and a DEXH-box helicase to direct RNAi

in *C. elegans*.  
 AUTHOR: Tabara Hiroaki; Yigit Erbay; Siomi Haruhiko; Mello Craig C  
 CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts  
 Medical School, Worcester, MA 1605, USA.  
 CONTRACT NUMBER: GM58800 (NIGMS)  
 SOURCE: Cell, (2002 Jun 28) Vol. 109, No. 7, pp. 861-71.  
 Journal code: 0413066. ISSN: 0092-8674.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)  
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 OTHER SOURCE: GENBANK-AF480439; GENBANK-AF480440; GENBANK-AY071926  
 ENTRY MONTH: 200208  
 ENTRY DATE: Entered STN: 12 Jul 2002  
 Last Updated on STN: 13 Aug 2002  
 Entered Medline: 12 Aug 2002

AB Double-stranded (ds) RNA induces potent gene silencing, termed RNA interference (RNAi). At an early step in RNAi, an RNaseIII-related enzyme, Dicer (DCR-1), processes long-trigger dsRNA into small interfering RNAs (siRNAs). DCR-1 is also required for processing endogenous regulatory RNAs called miRNAs, but how DCR-1 recognizes its endogenous and foreign substrates is not yet understood. Here we show that the *C. elegans* RNAi pathway gene, *rde-4*, encodes a dsRNA binding protein that interacts during RNAi with RNA identical to the trigger dsRNA. RDE-4 protein also interacts in vivo with DCR-1, RDE-1, and a conserved DEXH-box helicase. Our findings suggest a model in which RDE-4 and RDE-1 function together to detect and retain foreign dsRNA and to present this dsRNA to DCR-1 for processing.

L6 ANSWER 24 OF 36 HCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2002:914003 HCAPLUS  
 DOCUMENT NUMBER: 138:333205  
 TITLE: RNAi and related mechanisms and their potential use  
 for therapy  
 AUTHOR(S): Agami, Reuven  
 CORPORATE SOURCE: Division of Tumor Biology and Center for Biomedical  
 Genetics, The Netherlands Cancer Institute, Amsterdam,  
 1066 CX, Neth.  
 SOURCE: Current Opinion in Chemical Biology (2002), 6(6),  
 829-834  
 CODEN: COCBF4; ISSN: 1367-5931  
 PUBLISHER: Elsevier Science Ltd.  
 DOCUMENT TYPE: Journal; General Review  
 LANGUAGE: English

AB A review. Introduction of double-stranded RNAs into cells can suppress gene expression by mechanisms such as mRNA degradation or inhibition of translation. In mammalian cells, these two responses intersect, a feature that was recently used for the development of novel tools for stable and specific gene inactivation. These new tools were successfully applied to inhibit tumorigenicity and viral replication. Future development of appropriate in vivo delivery systems may make this technol. useful for disease therapy. Introduction of double-stranded RNAs into cells can suppress gene expression. This has recently found application in the development of novel tools for stable and specific gene inactivation. These new tools were successfully applied to inhibit tumorigenicity and viral replication.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 25 OF 36 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights

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ACCESSION NUMBER: 2002047852 EMBASE  
TITLE: RNA helicase mut-14-dependent gene silencing triggered in  
C. elegans by short antisense RNAs.  
AUTHOR: Tijsterman M.; Ketting R.F.; Okihara K.L.; Sijen T.;  
Plasterk R.H.A.  
CORPORATE SOURCE: R.H.A. Plasterk, Hubrecht Laboratory, Uppsalalaan 8, 3584  
CT, Utrecht, Netherlands. plasterk@niob.knaw.nl  
SOURCE: Science, (25 Jan 2002) Vol. 295, No. 5555, pp. 694-697. .  
Refs: 30  
ISSN: 0036-8075 CODEN: SCIEAS  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 004 Microbiology  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 14 Feb 2002  
Last Updated on STN: 14 Feb 2002

AB Posttranscriptional gene silencing in *Caenorhabditis elegans* results from exposure to double-stranded RNA (dsRNA), a phenomenon designated as RNA interference (RNAi), or from co-suppression, in which transgenic DNA leads to silencing of both the transgene and the endogenous gene. Here we show that single-stranded RNA oligomers of antisense polarity can also be potent inducers of gene silencing. As is the case for co-suppression, antisense RNAs act independently of the RNAi genes *rde-1* and *rde-4* but require the mutator/RNAi gene *mut-7* and a putative DEAD box RNA helicase, *mut-14*. Our data favor the hypothesis that gene silencing is accomplished by RNA primer extension using the mRNA as template, leading to dsRNA that is subsequently degraded.

L6 ANSWER 26 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:325987 SCISEARCH  
THE GENUINE ARTICLE: 537ZC  
TITLE: Fertile hypomorphic ARGONAUTE (*ago1*) mutants impaired in post-transcriptional gene silencing and virus resistance  
AUTHOR: Morel J B; Godon C; Mourrain P; Beclin C; Boutet S; Feuerbach F; Proux F; Vaucheret H (Reprint)  
CORPORATE SOURCE: INRA, Biol Cellulaire Lab, F-78026 Versailles, France (Reprint)  
COUNTRY OF AUTHOR: France  
SOURCE: PLANT CELL, (MAR 2002) Vol. 14, No. 3, pp. 629-639.  
ISSN: 1040-4651.  
PUBLISHER: AMER SOC PLANT BIOLOGISTS, 15501 MONONA DRIVE, ROCKVILLE, MD 20855 USA.  
DOCUMENT TYPE: Article; Journal  
LANGUAGE: English  
REFERENCE COUNT: 44  
ENTRY DATE: Entered STN: 26 Apr 2002  
Last Updated on STN: 26 Apr 2002

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Transgene-induced post-transcriptional gene silencing (PTGS) results from specific degradation of RNAs that are homologous with the transgene transcribed sequence. This phenomenon, also known as cosuppression in plants and quelling in fungi, resembles RNA interference (RNAi) in animals. Indeed, cosuppression/quelling/RNAi require related PAZ/PIWI proteins (*AGO1/QDE-2/RDE-1*), indicating that these mechanisms are related. Unlike *Neurospora crassa qde-2* and *Caenorhabditis elegans rde-1* mutants, which are morphologically normal, the 24 known *Arabidopsis ago1* mutants display severe developmental abnormalities and are sterile. Here, we report the isolation of hypomorphic *ago 1* mutants, including fertile ones. We show that these hypomorphic *ago1* mutants are defective for PTGS, like null

sgs2, sgs3, and agol mutants, suggesting that PTGS is more sensitive than development to perturbations in AGO1. Conversely, a mutation in ZWILLE/PINHEAD, another member of the Arabidopsis AGO1 gene family, affects development but not PTGS. Similarly, mutations in ALG-1 and ALG-2, two members of the C. elegans RDE-1 gene family, affect development but not RNAi, indicating that the control of PTGS/RNAi and development by PAZ/PIWI proteins can be uncoupled. Finally, we show that hypomorphic agol mutants are hypersensitive to virus infection, confirming the hypothesis that in plants PTGS is a mechanism of defense against viruses.

L6 ANSWER 27 OF 36 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:200342 SCISEARCH  
 THE GENUINE ARTICLE: 525WT  
 TITLE: RNA interference in the pathogenic fungus *Cryptococcus neoformans*  
 AUTHOR: Liu H; Cottrell T R; Pierini L M; Goldman W E; Doering T L (Reprint)  
 CORPORATE SOURCE: Campus Box 8230, 660 S Euclid Ave, St Louis, MO 63110 USA (Reprint); Washington Univ, Sch Med, Dept Mol Microbiol, St Louis, MO 63110 USA; Cornell Univ, Weill Med Coll, Dept Biochem, New York, NY 10021 USA  
 COUNTRY OF AUTHOR: USA  
 SOURCE: GENETICS, (FEB 2002) Vol. 160, No. 2, pp. 463-470. ISSN: 0016-6731.  
 PUBLISHER: GENETICS, 428 EAST PRESTON ST, BALTIMORE, MD 21202 USA.  
 DOCUMENT TYPE: Article; Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 40  
 ENTRY DATE: Entered STN: 15 Mar 2002  
 Last Updated on STN: 15 Mar 2002

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB *Cryptococcus neoformans* is a pathogenic fungus responsible for serious disease in immunocompromised individuals. This organism has recently been developed as an experimental system, with initiation of a genome project among other molecular advances. However, investigations of *Cryptococcus* are hampered by the technical difficulty of specific gene replacements. RNA interference, a process in which the presence of double-stranded RNA homologous to a gene of interest results in specific degradation of the corresponding message, may help solve this problem. We have shown that expression of double-stranded RNA corresponding to portions of the cryptococcal CAP59 and ADE2 genes results in reduced mRNA levels for those genes, with phenotypic consequences similar to that of gene disruption. The two genes could also be subjected to simultaneous interference through expression of chimeric double-stranded RNA. Specific modulation of protein expression through introduction of double-stranded RNA thus operates in *C. neoformans*, which is the first demonstration of this technique in a fungal organism. Use of RNA interference in *Cryptococcus* should allow manipulation of mRNA levels for functional analysis of genes of interest and enable efficient exploration of genes discovered by genome sequencing.

L6 ANSWER 28 OF 36 MEDLINE on STN DUPLICATE 8  
 ACCESSION NUMBER: 2002120843 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 11835276  
 TITLE: Control of developmental timing by small temporal RNAs: a paradigm for RNA-mediated regulation of gene expression.  
 AUTHOR: Banerjee Diya; Slack Frank  
 CORPORATE SOURCE: Department of Molecular, Cellular and Development Biology, Yale University, 266 Whitney Ave., New Haven, CT 06520, USA.  
 SOURCE: BioEssays : news and reviews in molecular, cellular and

developmental biology, (2002 Feb) Vol. 24, No. 2, pp.  
119-29. Ref: 61  
Journal code: 8510851. ISSN: 0265-9247.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200207  
ENTRY DATE: Entered STN: 22 Feb 2002  
Last Updated on STN: 2 Jul 2002  
Entered Medline: 1 Jul 2002  
AB Heterochronic genes control the timing of developmental programs. In *C. elegans*, two key genes in the heterochronic pathway, *lin-4* and *let-7*, encode small temporally expressed RNAs (stRNAs) that are not translated into protein. These stRNAs exert negative post-transcriptional regulation by binding to complementary sequences in the 3' untranslated regions of their target genes. stRNAs are transcribed as longer precursor RNAs that are processed by the RNase Dicer/DCR-1 and members of the RDE-1/AGO1 family of proteins, which are better known for their roles in RNA interference (RNAi). However, stRNA function appears unrelated to RNAi. Both sequence and temporal regulation of *let-7* stRNA is conserved in other animal species suggesting that this is an evolutionarily ancient gene. Indeed, *C. elegans*, *Drosophila* and humans encode at least 86 other RNAs with similar structural features to *lin-4* and *let-7*. We postulate that other small non-coding RNAs may function as stRNAs to control temporal identity during development in *C. elegans* and other organisms.  
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L6 ANSWER 29 OF 36 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN  
ACCESSION NUMBER: 2001-10403 BIOTECHDS  
TITLE: Novel RNA interference pathway genes and  
their protein products involved in mediation of genetic  
interference, useful for modulating and studying regulation  
of RNA interference pathway;  
transgenic animal  
AUTHOR: Mello C C; Fire A; Tabara H; Grishok A  
PATENT ASSIGNEE: Univ.Massachusetts; Carnegie-Inst.Washington  
LOCATION: Boston, MA, USA; Baltimore, MD, USA.  
PATENT INFO: WO 2001029058 26 Apr 2001  
APPLICATION INFO: WO 2000-US28470 13 Oct 2000  
PRIORITY INFO: US 2000-193218 30 Mar 2000; US 1999-159776 15 Oct 1999  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2001-316239 [33]  
AB An isolated nucleic acid (NA) molecule (I) comprising a nucleotide  
sequence encoding RNA interference pathway protein  
products RDE-1 and RDE-4 is claimed. NA encoding  
RDE-1 hybridizes under high stringency conditions to a  
NA sequence of Genbank Number AF180730 (of 3,207 bp, disclosed), GenBank  
Z83113.1 or their complements and NA encoding RDE-4 hybridizes with a  
sequence of 1,222 bp or its complement (disclosed). Also claimed are: a  
substantially pure RDE-1 or RDE-4 protein encoded by  
(I); an antibody specific for RDE-1 or RDE-4;  
enhancing expression of a transgene in a cell by reducing the  
activity of the RNA interference pathway; and  
inhibiting the activity of a gene by introducing RNA  
interference pathway agent into a cell where the ds RNA component  
of the RNA interference agent is targeted to the  
gene. Knockout strains of *Caenorhabditis elegans* containing the genes  
and antibodies are disclosed. RDE-1 protein  
comprises 1,020 amino acids (disclosed). RDE-1 and  
RDE-4 are prepared by recombinant techniques. (76pp)

L6 ANSWER 30 OF 36 MEDLINE on STN DUPLICATE 9

ACCESSION NUMBER: 2001544486 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11591334

TITLE: RNA interference: it's a small RNA world.

AUTHOR: Moss E G

CORPORATE SOURCE: Cell and Developmental Biology, Fox Chase Cancer Center, Philadelphia, PA 19111, USA.

SOURCE: Current biology : CB, (2001 Oct 2) Vol. 11, No. 19, pp. R772-5. Ref: 29  
Journal code: 9107782. ISSN: 0960-9822.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200201

ENTRY DATE: Entered STN: 10 Oct 2001  
Last Updated on STN: 11 Dec 2002  
Entered Medline: 2 Jan 2002

AB Short RNAs regulate gene expression in many species. Some are generated from any double-stranded RNA and degrade complementary RNAs; others are encoded by genes and repress specific mRNAs. Both, it turns out, are processed and handled by similar proteins. These pathways offer a glimpse into a world of small RNAs.

L6 ANSWER 31 OF 36 MEDLINE on STN DUPLICATE 10

ACCESSION NUMBER: 2001412025 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11461699

TITLE: Genes and mechanisms related to RNA interference regulate expression of the small temporal RNAs that control C. elegans developmental timing.

AUTHOR: Grishok A; Pasquinelli A E; Conte D; Li N; Parrish S; Ha I; Baillie D L; Fire A; Ruvkun G; Mello C C

CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, MA 01605, USA.

CONTRACT NUMBER: GM07321 (NIGMS)  
GM37706 (NIGMS)  
GM58800 (NIGMS)

SOURCE: Cell, (2001 Jul 13) Vol. 106, No. 1, pp. 23-34.  
Journal code: 0413066. ISSN: 0092-8674.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200108

ENTRY DATE: Entered STN: 13 Aug 2001  
Last Updated on STN: 13 Aug 2001  
Entered Medline: 9 Aug 2001

AB RNAi is a gene-silencing phenomenon triggered by double-stranded (ds) RNA and involves the generation of 21 to 26 nt RNA segments that guide mRNA destruction. In Caenorhabditis elegans, lin-4 and let-7 encode small temporal RNAs (stRNAs) of 22 nt that regulate stage-specific development. Here we show that inactivation of genes related to RNAi pathway genes, a homolog of Drosophila Dicer (dcr-1), and two homologs of rde-1 (alg-1 and alg-2), cause heterochronic phenotypes similar to lin-4 and let-7 mutations. Further we show that dcr-1, alg-1, and alg-2 are necessary for the maturation and activity of the lin-4 and let-7 stRNAs. Our findings suggest that a common processing machinery generates guide RNAs that mediate both RNAi and endogenous gene regulation.

L6 ANSWER 32 OF 36 MEDLINE on STN DUPLICATE 11  
 ACCESSION NUMBER: 2001022703 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 11016954  
 TITLE: AGO1, QDE-2, and RDE-1 are related  
 proteins required for post-transcriptional gene silencing  
 in plants, quelling in fungi, and RNA  
 interference in animals.  
 AUTHOR: Fagard M; Boutet S; Morel J B; Bellini C; Vaucheret H  
 CORPORATE SOURCE: Laboratoire de Biologie Cellulaire, Institut National de la  
 Recherche Agronomique, 78026 Versailles Cedex, France.  
 SOURCE: Proceedings of the National Academy of Sciences of the  
 United States of America, (2000 Oct 10) Vol. 97, No. 21,  
 pp. 11650-4.  
 Journal code: 7505876. ISSN: 0027-8424.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200011  
 ENTRY DATE: Entered STN: 22 Mar 2001  
 Last Updated on STN: 22 Mar 2001  
 Entered Medline: 9 Nov 2000

AB Introduction of transgene DNA may lead to specific degradation of RNAs  
 that are homologous to the transgene transcribed sequence through  
 phenomena named post-transcriptional gene silencing (PTGS) in plants,  
 quelling in fungi, and RNA interference (RNAi) in  
 animals. It was shown previously that PTGS, quelling, and RNAi require a  
 set of related proteins (SGS2, QDE-1, and EGO-1, respectively). Here we  
 report the isolation of Arabidopsis mutants impaired in PTGS which are  
 affected at the Argonautel (AGO1) locus. AGO1 is similar to QDE-2  
 required for quelling and RDE-1 required for RNAi.  
 Sequencing of ago1 mutants revealed one amino acid essential for PTGS that  
 is also present in QDE-2 and RDE-1 in a highly  
 conserved motif. Taken together, these results confirm the hypothesis  
 that these processes derive from a common ancestral mechanism that  
 controls expression of invading nucleic acid molecules at the  
 post-transcriptional level. As opposed to rde-1 and  
 qde-2 mutants, which are viable, ago1 mutants display several  
 developmental abnormalities, including sterility. These results raise the  
 possibility that PTGS, or at least some of its elements, could participate  
 in the regulation of gene expression during development in  
 plants.

L6 ANSWER 33 OF 36 MEDLINE on STN  
 ACCESSION NUMBER: 2000222265 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 10766620  
 TITLE: Molecular biology. RNA interference.  
 AUTHOR: Sharp P A; Zamore P D  
 CORPORATE SOURCE: Center for Cancer Research, Massachusetts Institute of  
 Technology, Cambridge, MA 02139, USA.. sharppa@mit.edu  
 SOURCE: Science (New York, N.Y.), (2000 Mar 31) Vol. 287, No. 5462,  
 pp. 2431-3.  
 Journal code: 0404511. ISSN: 0036-8075.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200004  
 ENTRY DATE: Entered STN: 21 Apr 2000  
 Last Updated on STN: 21 Apr 2000  
 Entered Medline: 11 Apr 2000



L6 ANSWER 34 OF 36 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on  
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ACCESSION NUMBER: 2000:346449 BIOSIS  
DOCUMENT NUMBER: PREV200000346449  
TITLE: Interfering with gene expression.  
AUTHOR(S): Marx, Jean  
SOURCE: Science (Washington D C), (26 May, 2000) Vol. 288, No.  
5470, pp. 1370-1372. print.  
CODEN: SCIEAS. ISSN: 0036-8075.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 16 Aug 2000  
Last Updated on STN: 7 Jan 2002

AB An explosion of recent evidence is revealing a new cellular pathway for  
silencing specific genes at the messenger RNA level that may protect  
organisms against viruses and genetic damage.

L6 ANSWER 35 OF 36 MEDLINE on STN

ACCESSION NUMBER: 2000210772 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10749214  
TITLE: A genetic link between co-suppression and RNA  
interference in *C. elegans*.  
AUTHOR: Ketting R F; Plasterk R H  
CORPORATE SOURCE: Division of Molecular Biology, The Netherlands Cancer  
Institute, Centre for Biomedical Genetics, Amsterdam.  
SOURCE: Nature, (2000 Mar 16) Vol. 404, No. 6775, pp. 296-8.  
Journal code: 0410462. ISSN: 0028-0836.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200004  
ENTRY DATE: Entered STN: 21 Apr 2000  
Last Updated on STN: 21 Apr 2000  
Entered Medline: 12 Apr 2000

AB Originally discovered in plants, the phenomenon of co-suppression by  
transgenic DNA has since been observed in many organisms from fungi to  
animals: introduction of transgenic copies of a gene results in reduced  
expression of the transgene as well as the endogenous gene. The  
effect depends on sequence identity between transgene and endogenous gene.  
Some cases of co-suppression resemble RNA interference  
(the experimental silencing of genes by the introduction of  
double-stranded RNA), as RNA seems to be both an important initiator and a  
target in these processes. Here we show that co-suppression in  
*Caenorhabditis elegans* is also probably mediated by RNA molecules. Both  
RNA interference and co-suppression have been implicated  
in the silencing of transposons. We now report that mutants of *C. elegans*  
that are defective in transposon silencing and RNA  
interference (mut-2, mut-7, mut-8 and mut-9) are in addition  
resistant to co-suppression. This indicates that RNA  
interference and co-suppression in *C. elegans* may be mediated at  
least in part by the same molecular machinery, possibly through RNA-guided  
degradation of messenger RNA molecules.

L6 ANSWER 36 OF 36 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights  
reserved on STN DUPLICATE 12

ACCESSION NUMBER: 1999365904 EMBASE  
TITLE: The *rde-1* gene, RNA  
interference, and transposon silencing in *C.*  
*elegans*.  
AUTHOR: Tabara H.; Sarkissian M.; Kelly W.G.; Fleenor J.; Grishok  
A.; Timmons L.; Fire A.; Mello C.C.  
CORPORATE SOURCE: H. Tabara, Department of Cell Biology, Program in Molecular  
Medicine, Univ. of Massachusetts Cancer Center, Worcester,

SOURCE: MA 01605, United States. craig.mello@ummed.edu  
Cell, (1999) Vol. 99, No. 2, pp. 123-132. .  
Refs: 57  
ISSN: 0092-8674 CODEN: CELLB5  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 002 Physiology  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 4 Nov 1999  
Last Updated on STN: 4 Nov 1999

AB Double-stranded (ds) RNA can induce sequence-specific inhibition of gene function in several organisms. However, both the mechanism and the physiological role of the interference process remain mysterious. In order to study the interference process, we have selected *C. elegans* mutants resistant to dsRNA-mediated interference (RNAi). Two loci, *rde-1* and *rde-4*, are defined by mutants strongly resistant to RNAi but with no obvious defects in growth or development. We show that *rde-1* is a member of the *piwi/sting/argonaute/zwiller/elf2C* gene family conserved from plants to vertebrates. Interestingly, several, but not all, RNAi-deficient strains exhibit mobilization of the endogenous transposons. We discuss implications for the mechanism of RNAi and the possibility that one natural function of RNAi is transposon silencing.

=> d his

(FILE 'HOME' ENTERED AT 09:22:04 ON 25 MAY 2007)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 09:30:52 ON 25 MAY 2007

L1 183 S "RDE-1"  
L2 48776 S RANI OR (RNA (W) INTERFERENCE)  
L3 131 S L1 AND L2  
L4 8397838 S CLON? OR EXPRESS? OR RECOMBINANT  
L5 69 S L3 AND L4  
L6 36 DUP REM L5 (33 DUPLICATES REMOVED)

=> e mello g c/au

E1 1 MELLO G B D/AU  
E2 1 MELLO G BRITTO/AU  
E3 6 --> MELLO G C/AU  
E4 1 MELLO G C R O T/AU  
E5 2 MELLO G F P/AU  
E6 2 MELLO G J P/AU  
E7 2 MELLO G K/AU  
E8 5 MELLO G P S/AU  
E9 1 MELLO G S/AU  
E10 1 MELLO G S B/AU  
E11 2 MELLO G W/AU  
E12 1 MELLO GARCIA FLAVIO ROBERTO/AU

=> s e3

L7 6 "MELLO G C"/AU

=> e fire a/au

E1 1 FIRDUS NEDZAD/AU  
E2 2 FIRE/AU  
E3 300 --> FIRE A/AU  
E4 1 FIRE A \*/AU  
E5 14 FIRE A Z/AU  
E6 150 FIRE ANDREW/AU  
E7 15 FIRE ANDREW Z/AU

E8	1	FIRE ANDY/AU
E9	1	FIRE C/AU
E10	2	FIRE D/AU
E11	23	FIRE E/AU
E12	11	FIRE ELLA/AU

=> s e3

L8 300 "FIRE A"/AU

=> e tabara h/au

E1	1	TABARA E/AU
E2	5	TABARA ELEONORA/AU
E3	126 -->	TABARA H/AU
E4	15	TABARA HIDEKI/AU
E5	31	TABARA HIROAKI/AU
E6	1	TABARA HIROKAI/AU
E7	7	TABARA HIROTO/AU
E8	1	TABARA HISAO/AU
E9	2	TABARA I/AU
E10	2	TABARA ISAO/AU
E11	1	TABARA ISTVAN/AU
E12	9	TABARA J/AU

=> s e3-e5

L9 172 ("TABARA H"/AU OR "TABARA HIDEKI"/AU OR "TABARA HIROAKI"/AU)

=> e grishok a/au

E1	1	GRISHNYAK V G/AU
E2	2	GRISHNYAKOV S B/AU
E3	38 -->	GRISHOK A/AU
E4	2	GRISHOK A A/AU
E5	27	GRISHOK ALLA/AU
E6	2	GRISHOK L P/AU
E7	1	GRISHOLD W/AU
E8	3	GRISHOM J/AU
E9	1	GRISHONKOV G YU/AU
E10	2	GRISHOV F I/AU
E11	1	GRISHOV VALERIJ A/AU
E12	9	GRISHOVA A I/AU

=> s e3-e5

L10 67 ("GRISHOK A"/AU OR "GRISHOK A A"/AU OR "GRISHOK ALLA"/AU)

=> d his

(FILE 'HOME' ENTERED AT 09:22:04 ON 25 MAY 2007)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 09:30:52 ON 25 MAY 2007

L1	183 S	"RDE-1"
L2	48776 S	RANI OR (RNA (W) INTERFERENCE)
L3	131 S	L1 AND L2
L4	8397838 S	CLON? OR EXPRESS? OR RECOMBINANT
L5	69 S	L3 AND L4
L6	36 DUP REM	L5 (33 DUPLICATES REMOVED)
		E MELLO G C/AU
L7	6 S	E3
		E FIRE A/AU
L8	300 S	E3
		E TABARA H/AU
L9	172 S	E3-E5
		E GRISHOK A/AU
L10	67 S	E3-E5

=> s 17 or 18 or 19 or 110  
L11 512 L7 OR L8 OR L9 OR L10

=> s 11 and 111  
L12 46 L1 AND L11

=> dup rem 112  
PROCESSING COMPLETED FOR L12  
L13 13 DUP REM L12 (33 DUPLICATES REMOVED)

=> d 1-13 ibib ab

L13 ANSWER 1 OF 13 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN  
ACCESSION NUMBER: 2006:380482 BIOSIS  
DOCUMENT NUMBER: PREV200600385781  
TITLE: RNAi beginnings, overview of the pathway in C-elegans.  
AUTHOR(S): Grishok, Alla [Reprint Author]  
CORPORATE SOURCE: MIT, Ctr Canc Res, 40 Ames St, Cambridge, MA 02139 USA  
agrishok@mit.edu  
SOURCE: Appasani, K [Editor]. (2005) pp. 17-28. RNA Interference  
Technology: From Basic Science to Drug Development.  
Publisher: CAMBRIDGE UNIV PRESS, 40 WEST 20TH ST, NEW YORK,  
NY 10011 USA.  
ISBN: 0-521-83677-8(H).  
DOCUMENT TYPE: Book; (Book Chapter)  
LANGUAGE: English  
ENTRY DATE: Entered STN: 2 Aug 2006  
Last Updated on STN: 2 Aug 2006

L13 ANSWER 2 OF 13 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2005137829 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 15741313  
TITLE: Transcriptional silencing of a transgene by RNAi in the  
soma of C. elegans.  
AUTHOR: Grishok Alla; Sinskey Jina L; Sharp Phillip A  
CORPORATE SOURCE: Center for Cancer Research, McGovern Institute,  
Massachusetts Institute of Technology, Cambridge,  
Massachusetts 02139, USA.  
CONTRACT NUMBER: P01-CA42063 (NCI)  
P30-CA 14051 (NCI)  
R37-GM34277 (NIGMS)  
SOURCE: Genes & development, (2005 Mar 15) Vol. 19, No. 6, pp.  
683-96. Electronic Publication: 2005-03-01.  
Journal code: 8711660. ISSN: 0890-9369.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: (COMPARATIVE STUDY)  
Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200504  
ENTRY DATE: Entered STN: 17 Mar 2005  
Last Updated on STN: 19 Apr 2005  
Entered Medline: 18 Apr 2005

AB The silencing of transgene expression at the level of transcription in the  
soma of Caenorhabditis elegans through an RNAi-dependent pathway has not  
been previously characterized. Most gene silencing due to RNAi in C.  
elegans occurs at the post-transcriptional level. We observed  
transcriptional silencing when worms containing the elt-2::gfp/LacZ  
transgene were fed RNA produced from the commonly used L4440 vector. The  
transgene and the vector share plasmid backbone sequences. This transgene  
silencing depends on multiple RNAi pathway genes, including dcr-1,  
rde-1, rde-4, and rrf-1. Unlike post-transcriptional

gene silencing in worms, *elt-2::gfp/LacZ* silencing is dependent on the PAZ-PIWI protein Alg-1 and on the HPI homolog Hpl-2. The latter is a chromatin silencing factor, and expression of the transgene is inhibited at the level of intron-containing precursor mRNA. This inhibition is accompanied by a decrease in the acetylation of histones associated with the transgene. This transcriptional silencing in the soma can be distinguished from transgene silencing in the germline by its inability to be transmitted across generations and its dependence on the *rde-1* gene. We therefore define this type of silencing as RNAi-induced Transcriptional Gene Silencing (RNAi-TGS). Additional chromatin-modifying components affecting RNAi-TGS were identified in a candidate RNAi screen.

L13 ANSWER 3 OF 13 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN  
 ACCESSION NUMBER: 2005:229753 SCISEARCH  
 THE GENUINE ARTICLE: 901FC  
 TITLE: A member of the polymerase beta nucleotidyltransferase superfamily is required for RNA interference in *C-elegans*  
 AUTHOR: Chen C C G; Simard M J; Tabara H; Brownell D R; McCollough J A; Mello C C (Reprint)  
 CORPORATE SOURCE: Univ Massachusetts, Sch Med, Program Mol Med, Worcester, MA 01605 USA (Reprint); Univ Massachusetts, Sch Med, Howard Hughes Med Inst, Worcester, MA 01605 USA; Kyoto Univ, HMRO, Grad Sch Med, Kyoto 6068501, Japan  
 COUNTRY OF AUTHOR: USA; Japan  
 SOURCE: *CURRENT BIOLOGY*, (22 FEB 2005) Vol. 15, No. 4, pp. 378-383  
 ISSN: 0960-9822.  
 PUBLISHER: CELL PRESS, 1100 MASSACHUSETTS AVE, CAMBRIDGE, MA 02138 USA.  
 DOCUMENT TYPE: Article; Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 20  
 ENTRY DATE: Entered STN: 10 Mar 2005  
 Last Updated on STN: 10 Mar 2005  
 \*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB RNA interference (RNAi) is an ancient, highly conserved mechanism in which small RNA molecules (siRNAs) guide the sequence-specific silencing of gene expression [1]. Several silencing machinery protein components have been identified, including helicases, RNase-related proteins, double- and singlestranded RNA binding proteins, and RNA-dependent RNA polymerase-related proteins [2]. Work on these factors has led to the revelation that RNAi mechanisms intersect with cellular pathways required for development and fertility [3, 4]. Despite rapid progress in understanding key steps in the RNAi pathway, it is clear that many factors required for both RNAi and related developmental mechanisms have not yet been identified. Here, we report the characterization of the *C. elegans* gene *rde-3*. Genetic analysis of presumptive null alleles indicates that *rde-3* is required for siRNA accumulation and for efficient RNAi in all tissues, and it is essential for fertility and viability at high temperatures. RDE-3 contains conserved domains found in the polymerase beta nucleotidyltransferase superfamily, which includes conventional poly(A) polymerases, 2'-5' oligoadenylate synthetase (OAS), and yeast Trf4p [5]. These findings implicate a new enzymatic modality in RNAi and suggest possible models for the role of RDE-3 in the RNAi mechanism.

L13 ANSWER 4 OF 13 MEDLINE on STN DUPLICATE 2  
 ACCESSION NUMBER: 2005027594 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 15653635  
 TITLE: RDE-2 interacts with MUT-7 to mediate RNA interference in *Caenorhabditis elegans*.  
 AUTHOR: Tops Bastiaan B J; Tabara Hiroaki; Sijen Titia;

Simmer Femke; Mello Craig C; Plasterk Ronald H A; Ketting  
 Rene F  
 CORPORATE SOURCE: Hubrecht Laboratory, Centre for Biomedical Genetics  
 Uppsalaalaa 8, 3584 CT Utrecht, The Netherlands.  
 SOURCE: Nucleic acids research, (2005) Vol. 33, No. 1, pp. 347-55.  
 Electronic Publication: 2005-01-13.  
 Journal code: 0411011. E-ISSN: 1362-4962.  
 PUB. COUNTRY: England: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200502  
 ENTRY DATE: Entered STN: 19 Jan 2005  
 Last Updated on STN: 11 Feb 2005  
 Entered Medline: 10 Feb 2005

AB In *Caenorhabditis elegans*, the activity of transposable elements is repressed in the germline. One of the mechanisms involved in this repression is RNA interference (RNAi), a process in which dsRNA targets cleavage of mRNAs in a sequence-specific manner. The first gene found to be involved in RNAi and transposon silencing in *C.elegans* is *mut-7*, a gene encoding a putative exoribonuclease. Here, we show that the MUT-7 protein resides in complexes of approximately 250 kDa in the nucleus and in the cytosol. In addition, we find that upon triggering of RNAi the cytosolic MUT-7 complex increases in size. This increase is independent of the presence of target RNA, but does depend on the presence of RDE-1 and RDE-4, two proteins involved in small interfering RNA (siRNA) production. Finally, using a yeast two-hybrid screen, we identified RDE-2/MUT-8 as one of the other components of this complex. This protein is encoded by the *rde-2/mut-8* locus, previously implicated in RNAi and transposon silencing. Using genetic complementation analysis, we show that the interaction between these two proteins is required for efficient RNAi in vivo. Together these data support a role for the MUT-7/RDE-2 complex downstream of siRNA formation, but upstream of siRNA mediated target RNA recognition, possibly indicating a role in the siRNA amplification step.

L13 ANSWER 5 OF 13 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on  
 STN  
 ACCESSION NUMBER: 2003:636265 SCISEARCH  
 THE GENUINE ARTICLE: 701CB  
 TITLE: Inducible systemic RNA silencing in *Caenorhabditis elegans*  
 AUTHOR: Timmons L (Reprint); Tabara H; Mello C C; Fire A  
 Z  
 CORPORATE SOURCE: Univ Kansas, Dept Mol Biosci, Lawrence, KS 66045 USA  
 (Reprint); Univ Tokushima, Tokushima 7708503, Japan; Univ  
 Massachusetts, Sch Med, Howard Hughes Med Inst, Worcester,  
 MA 01605 USA; Univ Massachusetts, Sch Med, Dept Cell Biol,  
 Worcester, MA 01605 USA; Carnegie Inst Washington, Dept  
 Embryol, Baltimore, MD 21210 USA  
 COUNTRY OF AUTHOR: USA; Japan  
 SOURCE: MOLECULAR BIOLOGY OF THE CELL, (JUL 2003) Vol. 14, No. 7,  
 pp. 2972-2983.  
 ISSN: 1059-1524.  
 PUBLISHER: AMER SOC CELL BIOLOGY, 8120 WOODMONT AVE, STE 750,  
 BETHESDA, MD 20814-2755 USA.  
 DOCUMENT TYPE: Article; Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 58  
 ENTRY DATE: Entered STN: 8 Aug 2003  
 Last Updated on STN: 8 Aug 2003

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Introduction of double-stranded RNA (dsRNA) can elicit a gene-specific  
 RNA interference response in a variety of organisms and cell types. In

many cases, this response has a systemic character in that silencing of gene expression is observed in cells distal from the site of dsRNA delivery. The molecular mechanisms underlying the mobile nature of RNA silencing are unknown. For example, although cellular entry of dsRNA is possible, cellular exit of dsRNA from normal animal cells has not been directly observed. We provide evidence that transgenic strains of *Caenorhabditis elegans* transcribing dsRNA from a tissue-specific promoter do not exhibit comprehensive systemic RNA interference phenotypes. In these same animals, modifications of environmental conditions can result in more robust systemic RNA silencing. Additionally, we find that genetic mutations can influence the systemic character of RNA silencing in *C. elegans* and can separate mechanisms underlying systemic RNA silencing into tissue-specific components. These data suggest that trafficking of RNA silencing signals in *C. elegans* is regulated by specific physiological and genetic factors.

L13 ANSWER 6 OF 13 MEDLINE on STN DUPLICATE 3  
 ACCESSION NUMBER: 2002364170 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 12110183  
 TITLE: The dsRNA binding protein RDE-4 interacts with RDE-1, DCR-1, and a DEXH-box helicase to direct RNAi in *C. elegans*.  
 AUTHOR: Tabara Hiroaki; Yigit Erbay; Siomi Haruhiko; Mello Craig C  
 CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, MA 1605, USA.  
 CONTRACT NUMBER: GM58800 (NIGMS)  
 SOURCE: Cell, (2002 Jun 28) Vol. 109, No. 7, pp. 861-71. Journal code: 0413066. ISSN: 0092-8674.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)  
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 OTHER SOURCE: GENBANK-AF480439; GENBANK-AF480440; GENBANK-AY071926  
 ENTRY MONTH: 200208  
 ENTRY DATE: Entered STN: 12 Jul 2002  
 Last Updated on STN: 13 Aug 2002  
 Entered Medline: 12 Aug 2002  
 AB Double-stranded (ds) RNA induces potent gene silencing, termed RNA interference (RNAi). At an early step in RNAi, an RNaseIII-related enzyme, Dicer (DCR-1), processes long-trigger dsRNA into small interfering RNAs (siRNAs). DCR-1 is also required for processing endogenous regulatory RNAs called miRNAs, but how DCR-1 recognizes its endogenous and foreign substrates is not yet understood. Here we show that the *C. elegans* RNAi pathway gene, *rde-4*, encodes a dsRNA binding protein that interacts during RNAi with RNA identical to the trigger dsRNA. RDE-4 protein also interacts in vivo with DCR-1, RDE-1, and a conserved DEXH-box helicase. Our findings suggest a model in which RDE-4 and RDE-1 function together to detect and retain foreign dsRNA and to present this dsRNA to DCR-1 for processing.

L13 ANSWER 7 OF 13 MEDLINE on STN DUPLICATE 4  
 ACCESSION NUMBER: 2002198477 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 11931230  
 TITLE: RNAi (Nematodes: *Caenorhabditis elegans*).  
 AUTHOR: Grishok Alla; Mello Craig C  
 CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts Medical School, Worcester 01605, USA.  
 SOURCE: Advances in genetics, (2002) Vol. 46, pp. 339-60. Ref: 109 Journal code: 0370421. ISSN: 0065-2660.  
 PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200208  
ENTRY DATE: Entered STN: 5 Apr 2002  
Last Updated on STN: 7 Aug 2002  
Entered Medline: 6 Aug 2002

AB RNA interference in *Caenorhabditis elegans* is a type of homology dependent posttranscriptional gene silencing induced by dsRNA. In this chapter we describe the history of the discovery of RNAi, its systemic nature, inheritance, and connection to other homology-dependent silencing phenomena like co-suppression and transcriptional gene silencing. We discuss RNAi-deficient mutants in *C. elegans* as well as characterized components of the RNAi, pathway, the molecular mechanism of RNAi, and its possible role in development and immunity.

L13 ANSWER 8 OF 13 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN  
DUPLICATE 5

ACCESSION NUMBER: 2001-10403 BIOTECHDS

TITLE: Novel RNA interference pathway genes and their protein products involved in mediation of genetic interference, useful for modulating and studying regulation of RNA interference pathway;  
transgenic animal

AUTHOR: Mello C C; Fire A; Tabara H; Grishok A

PATENT ASSIGNEE: Univ.Massachusetts; Carnegie-Inst.Washington

LOCATION: Boston, MA, USA; Baltimore, MD, USA.

PATENT INFO: WO 2001029058 26 Apr 2001

APPLICATION INFO: WO 2000-US28470 13 Oct 2000

PRIORITY INFO: US 2000-193218 30 Mar 2000; US 1999-159776 15 Oct 1999

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2001-316239 [33]

AB An isolated nucleic acid (NA) molecule (I) comprising a nucleotide sequence encoding RNA interference pathway protein products RDE-1 and RDE-4 is claimed. NA encoding RDE-1 hybridizes under high stringency conditions to a NA sequence of Genbank Number AF180730 (of 3,207 bp, disclosed), GenBank Z83113.1 or their complements and NA encoding RDE-4 hybridizes with a sequence of 1,222 bp or its complement (disclosed). Also claimed are: a substantially pure RDE-1 or RDE-4 protein encoded by (I); an antibody specific for RDE-1 or RDE-4; enhancing expression of a transgene in a cell by reducing the activity of the RNA interference pathway; and inhibiting the activity of a gene by introducing RNA interference pathway agent into a cell where the ds RNA component of the RNA interference agent is targeted to the gene. Knockout strains of *Caenorhabditis elegans* containing the genes and antibodies are disclosed. RDE-1 protein comprises 1,020 amino acids (disclosed). RDE-1 and RDE-4 are prepared by recombinant techniques.  
(76pp)

L13 ANSWER 9 OF 13 MEDLINE on STN DUPLICATE 6

ACCESSION NUMBER: 2001574258 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11680844

TITLE: Distinct roles for RDE-1 and RDE-4 during RNA interference in *Caenorhabditis elegans*.

AUTHOR: Parrish S; Fire A

CORPORATE SOURCE: Department of Embryology, Carnegie Institution of Washington, Baltimore, Maryland 21210, USA.

CONTRACT NUMBER: GM07231 (NIGMS)

GM37706 (NIGMS)

SOURCE: RNA (New York, N.Y.), (2001 Oct) Vol. 7, No. 10, pp.



1397-402.

Journal code: 9509184. ISSN: 1355-8382.

PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200112  
ENTRY DATE: Entered STN: 30 Oct 2001  
Last Updated on STN: 23 Jan 2002  
Entered Medline: 4 Dec 2001

AB RNA interference (RNAi) is a cellular defense mechanism that uses double-stranded RNA (dsRNA) as a sequence-specific trigger to guide the degradation of homologous single-stranded RNAs. RNAi is a multistep process involving several proteins and at least one type of RNA intermediate, a population of small 21-25 nt RNAs (called siRNAs) that are initially derived from cleavage of the dsRNA trigger. Genetic screens in *Caenorhabditis elegans* have identified numerous mutations that cause partial or complete loss of RNAi. In this work, we analyzed cleavage of injected dsRNA to produce the initial siRNA population in animals mutant for *rde-1* and *rde-4*, two genes that are essential for RNAi but that are not required for organismal viability or fertility. Our results suggest distinct roles for RDE-1 and RDE-4 in the interference process. Although null mutants lacking *rde-1* show no phenotypic response to dsRNA, the amount of siRNAs generated from an injected dsRNA trigger was comparable to that of wild-type. By contrast, mutations in *rde-4* substantially reduced the population of siRNAs derived from an injected dsRNA trigger. Injection of chemically synthesized 24- or 25-nt siRNAs could circumvent RNAi resistance in *rde-4* mutants, whereas no bypass was observed in *rde-1* mutants. These results support a model in which RDE-4 is involved before or during production of siRNAs, whereas RDE-1 acts after the siRNAs have been formed.

L13 ANSWER 10 OF 13 MEDLINE on STN

DUPLICATE 7

ACCESSION NUMBER: 2001412025 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11461699  
TITLE: Genes and mechanisms related to RNA interference regulate expression of the small temporal RNAs that control *C. elegans* developmental timing.  
AUTHOR: Grishok A; Pasquinelli A E; Conte D; Li N; Parrish S; Ha I; Baillie D L; Fire A; Ruvkun G; Mello C C  
CORPORATE SOURCE: Program in Molecular Medicine, University of Massachusetts Medical School, Worcester, MA 01605, USA.  
CONTRACT NUMBER: GM07321 (NIGMS)  
GM37706 (NIGMS)  
GM58800 (NIGMS)  
SOURCE: Cell, (2001 Jul 13) Vol. 106, No. 1, pp. 23-34.  
Journal code: 0413066. ISSN: 0092-8674.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
(RESEARCH SUPPORT, NON-U.S. GOV'T)  
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200108  
ENTRY DATE: Entered STN: 13 Aug 2001  
Last Updated on STN: 13 Aug 2001  
Entered Medline: 9 Aug 2001

AB RNAi is a gene-silencing phenomenon triggered by double-stranded (ds) RNA and involves the generation of 21 to 26 nt RNA segments that guide mRNA destruction. In *Caenorhabditis elegans*, *lin-4* and *let-7* encode small

temporal RNAs (stRNAs) of 22 nt that regulate stage-specific development. Here we show that inactivation of genes related to RNAi pathway genes, a homolog of *Drosophila* Dicer (*dcr-1*), and two homologs of *rde-1* (*alg-1* and *alg-2*), cause heterochronic phenotypes similar to *lin-4* and *let-7* mutations. Further we show that *dcr-1*, *alg-1*, and *alg-2* are necessary for the maturation and activity of the *lin-4* and *let-7* stRNAs. Our findings suggest that a common processing machinery generates guide RNAs that mediate both RNAi and endogenous gene regulation.

L13 ANSWER 11 OF 13 MEDLINE on STN  
 ACCESSION NUMBER: 2000207007 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 10741970  
 TITLE: Genetic requirements for inheritance of RNAi in *C. elegans*.  
 AUTHOR: Grishok A; Tabara H; Mello C C  
 CORPORATE SOURCE: Program in Molecular Medicine, Department of Cell Biology, University of Massachusetts Cancer Center, Two Biotech Suite 213, 373 Plantation Street, Worcester, MA 01605, USA.  
 CONTRACT NUMBER: GM58800 (NIGMS)  
 SOURCE: Science (New York, N.Y.), (2000 Mar 31) Vol. 287, No. 5462, pp. 2494-7.  
 Journal code: 0404511. ISSN: 0036-8075.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Commentary  
 Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200004  
 ENTRY DATE: Entered STN: 21 Apr 2000  
 Last Updated on STN: 21 Apr 2000  
 Entered Medline: 11 Apr 2000

AB In *Caenorhabditis elegans*, the introduction of double-stranded RNA triggers sequence-specific genetic interference (RNAi) that is transmitted to offspring. The inheritance properties associated with this phenomenon were examined. Transmission of the interference effect occurred through a dominant extragenic agent. The wild-type activities of the RNAi pathway genes *rde-1* and *rde-4* were required for the formation of this interfering agent but were not needed for interference thereafter. In contrast, the *rde-2* and *mut-7* genes were required downstream for interference. These findings provide evidence for germ line transmission of an extragenic sequence-specific silencing factor and implicate *rde-1* and *rde-4* in the formation of the inherited agent.

L13 ANSWER 12 OF 13 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 8  
 ACCESSION NUMBER: 2000123929 EMBASE  
 TITLE: Genetic requirements for inheritance of RNAi in *C. elegans*.  
 AUTHOR: Grishok A.; Tabara H.; Mello C.C.  
 CORPORATE SOURCE: C.C. Mello, Program in Molecular Medicine, Department of Cell Biology, Univ. of Massachusetts Cancer Center, 373 Plantation Street, Worcester, MA 01605, United States.  
 SOURCE: Science, (31 Mar 2000) Vol. 287, No. 5462, pp. 2494-2497. .  
 ISSN: 0036-8075 CODEN: SCIEAS  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 004 Microbiology  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 21 Apr 2000  
 Last Updated on STN: 21 Apr 2000

AB In *Caenorhabditis elegans*, the introduction of double-stranded RNA triggers sequence-specific genetic interference (RNAi) that is transmitted

to offspring. The inheritance properties associated with this phenomenon were examined. Transmission of the interference effect occurred through a dominant extragenic agent. The wild-type activities of the RNAi pathway genes *rde-1* and *rde-4* were required for the formation of this interfering agent but were not needed for interference thereafter. In contrast, the *rde-2* and *mut-7* genes were required downstream for interference. These findings provide evidence for germ line transmission of an extragenic sequence-specific silencing factor and implicate *rde-1* and *rde-4* in the formation of the inherited agent.

L13 ANSWER 13 OF 13 MEDLINE on STN DUPLICATE 9  
 ACCESSION NUMBER: 2000004389 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 10535731  
 TITLE: The *rde-1* gene, RNA interference, and transposon silencing in *C. elegans*.  
 AUTHOR: Tabara H; Sarkissian M; Kelly W G; Fleenor J; Grishok A; Timmons L; Fire A; Mello C C  
 CORPORATE SOURCE: Department of Cell Biology, Program in Molecular Medicine, University of Massachusetts Cancer Center, Worcester 01605, USA.  
 CONTRACT NUMBER: GM37706 (NIGMS)  
 GM58800 (NIGMS)  
 HD08353 (NICHD)  
 SOURCE: Cell, (1999 Oct 15) Vol. 99, No. 2, pp. 123-32.  
 Journal code: 0413066. ISSN: 0092-8674.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 (RESEARCH SUPPORT, NON-U.S. GOV'T)  
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 OTHER SOURCE: GENBANK-AF180730  
 ENTRY MONTH: 199911  
 ENTRY DATE: Entered STN: 11 Jan 2000  
 Last Updated on STN: 11 Jan 2000  
 Entered Medline: 10 Nov 1999

AB Double-stranded (ds) RNA can induce sequence-specific inhibition of gene function in several organisms. However, both the mechanism and the physiological role of the interference process remain mysterious. In order to study the interference process, we have selected *C. elegans* mutants resistant to dsRNA-mediated interference (RNAi). Two loci, *rde-1* and *rde-4*, are defined by mutants strongly resistant to RNAi but with no obvious defects in growth or development. We show that *rde-1* is a member of the *piwi/sting/argonaute/zwiller/eIF2C* gene family conserved from plants to vertebrates. Interestingly, several, but not all, RNAi-deficient strains exhibit mobilization of the endogenous transposons. We discuss implications for the mechanism of RNAi and the possibility that one natural function of RNAi is transposon silencing.

=> d his

(FILE 'HOME' ENTERED AT 09:22:04 ON 25 MAY 2007)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 09:30:52 ON 25 MAY 2007

L1 183 S "RDE-1"  
 L2 48776 S RANI OR (RNA (W) INTERFERENCE)  
 L3 131 S L1 AND L2  
 L4 8397838 S CLON? OR EXPRESS? OR RECOMBINANT  
 L5 69 S L3 AND L4  
 L6 36 DUP REM L5 (33 DUPLICATES REMOVED)  
 E MELLO G C/AU

L7            6 S E3  
             E FIRE A/AU  
L8           300 S E3  
             E TABARA H/AU  
L9           172 S E3-E5  
             E GRISHOK A/AU  
L10          67 S E3-E5  
L11          512 S L7 OR L8 OR L9 OR L10  
L12          46 S L1 AND L11  
L13          13 DUP REM L12 (33 DUPLICATES REMOVED)

	Document ID	Kind Codes	Source	Issue Date	Pages	Title
1	US 2007009986 2 A1		US- PGPUB	20070503	68	siRNA targeting carbonic anhydrase II
2	US 2007009365 3 A1		US- PGPUB	20070426	68	siRNA targeting MCL1
3	US 2007009344 5 A1		US- PGPUB	20070426	60	RNA interference mediating small RNA molecules
4	US 2007008815 5 A1		US- PGPUB	20070419	145	siRNA targeting tumor necrosis factor superfamily member 1A
5	US 2007008815 4 A1		US- PGPUB	20070419	70	siRNA targeting complement factor B
6	US 2007008815 3 A1		US- PGPUB	20070419	70	siRNA targeting BCL2L1
7	US 2007008815 2 A1		US- PGPUB	20070419	151	siRNA targeting KRAS
8	US 2007007282 3 A1		US- PGPUB	20070329	70	siRNA targeting survivin
9	US 2007006788 0 A1		US- PGPUB	20070322	44	Isolation of Proteins Involved in Posttranscriptional Gene Silencing and Methods of Use
10	US 2007003907 2 A1		US- PGPUB	20070215	126	Functional and hyperfunctional siRNA
11	US 2007003366 3 A1		US- PGPUB	20070208	26	ES cells having enhanced RNAi effect
12	US 2007003184 4 A1		US- PGPUB	20070208	128	Functional and hyperfunctional siRNA
13	US 2007003141 7 A2		US- PGPUB	20070208	164	DICER INTERACTING PROTEINS AND USES THEREFOR
14	US 2007000396 3 A1		US- PGPUB	20070104	38	RNA sequence-specific mediators of RNA interference

	Document ID	Kind Codes	Source	Issue Date	Pages	Title
15	US 2007000396 2 A1		US- PGPUB	20070104	37	RNA sequence-specific mediators of RNA interference
16	US 2007000396 1 A1		US- PGPUB	20070104	37	RNA sequence-specific mediators of RNA interference
17	US 2007000396 0 A1		US- PGPUB	20070104	37	RNA sequence-specific mediators of RNA interference
18	US 2006028660 7 A1		US- PGPUB	20061221	44	Isolation of Proteins Involved in Posttranscriptional Gene Silencing and Methods of Use
19	US 2006027583 0 A1		US- PGPUB	20061207	44	Isolation of Proteins Involved in Posttranscriptional Gene Silencing and Methods of Use
20	US 2006027205 2 A1		US- PGPUB	20061130	44	Isolation of proteins involved in posttranscriptional gene silencing and methods of use
21	US 2006027204 7 A1		US- PGPUB	20061130	44	Isolation of proteins involved in posttranscriptional gene silencing and methods of use
22	US 2006026995 5 A1		US- PGPUB	20061130	44	Isolation of proteins involved in posttranscriptional gene silencing and methods of use
23	US 2006024107 2 A1		US- PGPUB	20061026	58	Oligomeric compounds for use in gene modulation
24	US 2006022836 1 A1		US- PGPUB	20061012	197	Dicer interacting proteins and uses therefor
25	US 2006015423 7 A1		US- PGPUB	20060713	46	Soluble rna polymerase protein and methods for the use thereof

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26	US 2006014373 7 A1		US- PGPUB	20060629	33	Method of controlling gene silencing using site specific recombination
27	US 2006014160 0 A1		US- PGPUB	20060629	189	Methods and compositions related to argonaute proteins
28	US 2006013545 6 A1		US- PGPUB	20060622	151	Methods and compositions for RNA interference
29	US 2006009021 7 A1		US- PGPUB	20060427	44	Isolation of proteins involved in posttranscriptional gene silencing and methods of use
30	US 2006003000 3 A1		US- PGPUB	20060209	13	Composition and method for introduction of RNA interference sequences into targeted cells and tissues
31	US 2006002479 8 A1		US- PGPUB	20060202	62	RNA interference pathway genes as tools for targeted genetic interference
32	US 2005026655 2 A1		US- PGPUB	20051201	87	Reagents and methods for identification of RNAi pathway genes and chemical modulators of RNAi
33	US 2005026075 5 A1		US- PGPUB	20051124	61	Sequential delivery of oligomeric compounds
34	US 2005026065 2 A1		US- PGPUB	20051124	134	Compositions and methods that modulate RNA interference
35	US 2005026021 4 A1		US- PGPUB	20051124	12	Composition and method for introduction of RNA interference sequences into targeted cells and tissues

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36	US 2005025548 7 A1		US- PGPUB	20051117	116	Methods and compositions for selecting siRNA of improved functionality
37	US 2005024679 4 A1		US- PGPUB	20051103	102	Functional and hyperfunctional siRNA
38	US 2005024547 5 A1		US- PGPUB	20051103	126	Functional and hyperfunctional siRNA directed against Bcl-2
39	US 2005023400 7 A1		US- PGPUB	20051020	59	RNA interference mediating small RNA molecules
40	US 2005023400 6 A1		US- PGPUB	20051020	59	RNA interference mediating small RNA molecules
41	US 2005022927 2 A1		US- PGPUB	20051013	23	Compositions and methods for gene silencing
42	US 2005022342 7 A1		US- PGPUB	20051006	107	Modified polynucleotides for reducing off-target effects in RNA interference
43	US 2005021485 1 A1		US- PGPUB	20050929	90	siRNA knockout assay method and constructs
44	US 2005020851 8 A1		US- PGPUB	20050922	32	Method and apparatus for determination of RNAi cell transfection effects by multiple gene expression analysis on micro-arrays
45	US 2005020442 7 A1		US- PGPUB	20050915	107	Polynucleotides and polypeptides involved in post-transcriptional gene silencing
46	US 2005020304 3 A1		US- PGPUB	20050915	159	Identification of toxic nucleotide sequences



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47	US 2005018658 6 A1		US- PGPUB	20050825	105	Methods and compositions for enhancing the efficacy and specificity of RNAi
48	US 2005018201 5 A1		US- PGPUB	20050818	67	Antisense modulation of EIF2C1 expression
49	US 2005018138 2 A1		US- PGPUB	20050818	99	Methods and compositions for enhancing the efficacy and specificity of RNAi
50	US 2005014333 2 A1		US- PGPUB	20050630	34	Compositions and processes using siRNA, amphipathic compounds and polycations
51	US 2005014258 1 A1		US- PGPUB	20050630	172	Microrna as ligands and target molecules
52	US 2005012395 2 A1		US- PGPUB	20050609	23	Methods of rapid detection and identification of bioagents using microRNA
53	US 2005010091 3 A1		US- PGPUB	20050512	61	RNA interference pathway genes as tools for targeted genetic interference
54	US 2005006989 6 A1		US- PGPUB	20050331	229	Rb pathway and chromatin remodeling genes that antagonize let-60 Ras signaling
55	US 2005005900 5 A1		US- PGPUB	20050317	146	Microrna molecules
56	US 2005004275 2 A1		US- PGPUB	20050224	14	Methods of inducing gene expression
57	US 2005003798 8 A1		US- PGPUB	20050217	42	Methods and compositions for controlling efficacy of RNA silencing

58	US 2005003738 7 A1		US- PGPUB	20050217	141	Modulation of the RNA interference pathway
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	Document ID	Kind Codes	Source	Issue Date	Pages	Title
59	US 2005002627 8 A1		US- PGPUB	20050203	63	RNA interference mediating small RNA molecules
60	US 2005001980 6 A1		US- PGPUB	20050127	31	Nucleic acids and polypeptides required for cell survival in the absence of Rb
61	US 2005000354 1 A1		US- PGPUB	20050106	26	ES cells having enhanced RNAi effect
62	US 2004026670 7 A1		US- PGPUB	20041230	159	Stabilized polynucleotides for use in RNA interference
63	US 2004026583 9 A1		US- PGPUB	20041230	61	RNA interference pathway genes as tools for targeted genetic interference
64	US 2004025924 8 A1		US- PGPUB	20041223	63	RNA interference mediating small RNA molecules
65	US 2004025924 7 A1		US- PGPUB	20041223	60	Rna interference mediating small rna molecules
66	US 2004022926 7 A1		US- PGPUB	20041118	86	Tumor suppressor pathway in C. elegans
67	US 2004022926 6 A1		US- PGPUB	20041118	60	RNA interference mediating small RNA molecules
68	US 2004022440 5 A1		US- PGPUB	20041111	57	siRNA induced systemic gene silencing in mammalian systems
69	US 2004019864 0 A1		US- PGPUB	20041007	66	Stabilized polynucleotides for use in RNA interference
70	US 2004018547 9 A1		US- PGPUB	20040923	49	Modified oligonucleotides for use in gene modulation

71	US 2004017628 2 A1		US- PGPUB	20040909	61	Cellular delivery and activation of polypeptide-nucleic acid complexes
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72	US 2004013757 2 A1		US- PGPUB	20040715	35	Compositions and methods for generating conditional knockouts
73	US 2004013749 0 A1		US- PGPUB	20040715	41	Methods for making polynucleotide libraries, polynucleotide arrays, and cell libraries for high-throughput genomics analysis
74	US 2004013706 4 A1		US- PGPUB	20040715	23	Compositions and processes using siRNA, amphipathic compounds and polycations
75	US 2004013298 4 A1		US- PGPUB	20040708	18	Antisense compounds, methods and compositions for treating NGAL-related inflammatory disorders
76	US 2004008753 3 A1		US- PGPUB	20040506	21	Antisense compounds, methods and compositions for treating MMP-12 related inflammatory disorders
77	US 2004008691 1 A1		US- PGPUB	20040506	35	Inhibition of gene expression in vertebrates using double-stranded RNA (RNAi)
78	US 2004008688 4 A1		US- PGPUB	20040506	126	Methods and compositions for RNA interference
79	US 2004004504 3 A1		US- PGPUB	20040304	38	Compositions and methods for generating conditional knockouts

80	US 2004001992 1 A1		US- PGPUB	20040129	42	Non-human mammal with disrupted or modified MIF gene, and uses thereof
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81	US 2004001900 8 A1		US- PGPUB	20040129	25	Compositions and processes using siRNA, amphipathic compounds and polycations
82	US 2004001899 9 A1		US- PGPUB	20040129	55	Methods and compositions for RNA interference
83	US 2003023244 2 A1		US- PGPUB	20031218	119	Antisense modulation of PAZ/PIWI domain-containing protein expression
84	US 2003019862 7 A1		US- PGPUB	20031023	90	siRNA knockout assay method and constructs
85	US 2003016749 0 A1		US- PGPUB	20030904	19	Gene silencing by systemic RNA interference
86	US 2003014359 7 A1		US- PGPUB	20030731	40	Methods for making polynucleotide libraries, polynucleotide arrays, and cell libraries for high-throughput genomics analysis
87	US 2003012528 1 A1		US- PGPUB	20030703	28	Compositions and processes using siRNA, amphipathic compounds and polycations
88	US 2003011440 9 A1		US- PGPUB	20030619	22	Facilitation of RNA interference
89	US 2003010892 3 A1		US- PGPUB	20030612	37	RNA sequence-specific mediators of RNA interference
90	US 2003010504 2 A1		US- PGPUB	20030605	66	Antisense modulation of EIF2C1 expression
91	US 2003009998 4 A1		US- PGPUB	20030529	44	Isolation of proteins involved in posttranscriptional gene silencing and methods of use

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92	US 2003008447 1 A1		US- PGPUB	20030501	74	Methods and compositions for RNA interference
93	US 2003007762 3 A1		US- PGPUB	20030424	107	Polynucleotides and polypeptides involved in post-transcriptional gene silencing
94	US 2002016212 6 A1		US- PGPUB	20021031	56	Methods and compositions for RNA interference
95	US 2002013790 6 A1		US- PGPUB	20020926	89	Tumor suppressor pathway in C. elegans
96	US 2002008635 6 A1		US- PGPUB	20020704	31	RNA sequence-specific mediators of RNA interference
97	US 7150969 B2		USPAT	20061219	31	Alternatively spliced isoform of acetyl-CoA carboxylase 2 (ACC2)
98	US 7101995 B2		USPAT	20060905	21	Compositions and processes using siRNA, amphipathic compounds and polycations
99	US 7078196 B2		USPAT	20060718	67	RNA interference mediating small RNA molecules
100	US 7056704 B2		USPAT	20060606	65	RNA interference mediating small RNA molecules
101	US 7001739 B2		USPAT	20060221	47	Isolation of proteins involved in posttranscriptional gene silencing and methods of use
102	US 6573099 B2		USPAT	20030603	46	Genetic constructs for delaying or repressing the expression of a target gene
103	US 6506559 B1		USPAT	20030114	24	Genetic inhibition by double-stranded RNA



	L #	Hits	Search Text
1	L1	150	"RDE-1"
2	L2	5926	"RNAi" or (RNA adj interference)
3	L3	150	l1 and l2
4	L4	1513 08	clon? or express? or recombinant
5	L5	114	l3 and l4
6	L6	4425	dsRNA
7	L7	103	l5 and l6
8	L8	1605 51	MELLO FIRE TABARA GRISHOK
9	L9	140	l1 and l8
10	L10	103	l1 and l7

	Document ID	Kind Codes	Source	Issue Date	Pages	Title
1	US 2007009986 2 A1		US- PGPUB	20070503	68	siRNA targeting carbonic anhydrase II
2	US 2007009365 3 A1		US- PGPUB	20070426	68	siRNA targeting MCL1
3	US 2007009344 5 A1		US- PGPUB	20070426	60	RNA interference mediating small RNA molecules
4	US 2007008815 5 A1		US- PGPUB	20070419	145	siRNA targeting tumor necrosis factor superfamily member 1A
5	US 2007008815 4 A1		US- PGPUB	20070419	70	siRNA targeting complement factor B
6	US 2007008815 3 A1		US- PGPUB	20070419	70	siRNA targeting BCL2L1
7	US 2007008815 2 A1		US- PGPUB	20070419	151	siRNA targeting KRAS
8	US 2007007282 3 A1		US- PGPUB	20070329	70	siRNA targeting survivin
9	US 2007006788 0 A1		US- PGPUB	20070322	44	Isolation of Proteins Involved in Posttranscriptional Gene Silencing and Methods of Use
10	US 2007003907 2 A1		US- PGPUB	20070215	126	Functional and hyperfunctional siRNA
11	US 2007003366 3 A1		US- PGPUB	20070208	26	ES cells having enhanced RNAi effect
12	US 2007003184 4 A1		US- PGPUB	20070208	128	Functional and hyperfunctional siRNA
13	US 2007003141 7 A2		US- PGPUB	20070208	164	DICER INTERACTING PROTEINS AND USES THEREFOR
14	US 2007000396 3 A1		US- PGPUB	20070104	38	RNA sequence-specific mediators of RNA interference

	Document ID	Kind Codes	Source	Issue Date	Pages	Title
15	US 2007000396 2 A1		US- PGPUB	20070104	37	RNA sequence-specific mediators of RNA interference
16	US 2007000396 1 A1		US- PGPUB	20070104	37	RNA sequence-specific mediators of RNA interference
17	US 2007000396 0 A1		US- PGPUB	20070104	37	RNA sequence-specific mediators of RNA interference
18	US 2006028660 7 A1		US- PGPUB	20061221	44	Isolation of Proteins Involved in Posttranscriptional Gene Silencing and Methods of Use
19	US 2006027583 0 A1		US- PGPUB	20061207	44	Isolation of Proteins Involved in Posttranscriptional Gene Silencing and Methods of Use
20	US 2006027205 2 A1		US- PGPUB	20061130	44	Isolation of proteins involved in posttranscriptional gene silencing and methods of use
21	US 2006027204 7 A1		US- PGPUB	20061130	44	Isolation of proteins involved in posttranscriptional gene silencing and methods of use
22	US 2006026995 5 A1		US- PGPUB	20061130	44	Isolation of proteins involved in posttranscriptional gene silencing and methods of use
23	US 2006024107 2 A1		US- PGPUB	20061026	58	Oligomeric compounds for use in gene modulation
24	US 2006022836 1 A1		US- PGPUB	20061012	197	Dicer interacting proteins and uses therefor
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32	US 2005026655 2 A1		US- PGPUB	20051201	87	Reagents and methods for identification of RNAi pathway genes and chemical modulators of RNAi
33	US 2005026075 5 A1		US- PGPUB	20051124	61	Sequential delivery of oligomeric compounds
34	US 2005026065 2 A1		US- PGPUB	20051124	134	Compositions and methods that modulate RNA interference
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38	US 2005024547 5 A1		US- PGPUB	20051103	126	Functional and hyperfunctional siRNA directed against Bcl-2
39	US 2005023400 7 A1		US- PGPUB	20051020	59	RNA interference mediating small RNA molecules
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41	US 2005022927 2 A1		US- PGPUB	20051013	23	Compositions and methods for gene silencing
42	US 2005022342 7 A1		US- PGPUB	20051006	107	Modified polynucleotides for reducing off-target effects in RNA interference
43	US 2005021485 1 A1		US- PGPUB	20050929	90	siRNA knockout assay method and constructs
44	US 2005020851 8 A1		US- PGPUB	20050922	32	Method and apparatus for determination of RNAi cell transfection effects by multiple gene expression analysis on micro-arrays
45	US 2005020442 7 A1		US- PGPUB	20050915	107	Polynucleotides and polypeptides involved in post-transcriptional gene silencing
46	US 2005020304 3 A1		US- PGPUB	20050915	159	Identification of toxic nucleotide sequences

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49	US 2005018138 2 A1		US- PGPUB	20050818	99	Methods and compositions for enhancing the efficacy and specificity of RNAi
50	US 2005014333 2 A1		US- PGPUB	20050630	34	Compositions and processes using siRNA, amphipathic compounds and polycations
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52	US 2005012395 2 A1		US- PGPUB	20050609	23	Methods of rapid detection and identification of bioagents using microRNA
53	US 2005010091 3 A1		US- PGPUB	20050512	61	RNA interference pathway genes as tools for targeted genetic interference
54	US 2005006989 6 A1		US- PGPUB	20050331	229	Rb pathway and chromatin remodeling genes that antagonize let-60 Ras signaling
55	US 2005005900 5 A1		US- PGPUB	20050317	146	Microrna molecules
56	US 2005004275 2 A1		US- PGPUB	20050224	14	Methods of inducing gene expression
57	US 2005003798 8 A1		US- PGPUB	20050217	42	Methods and compositions for controlling efficacy of RNA silencing

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61	US 2005000354 1 A1		US- PGPUB	20050106	26	ES cells having enhanced RNAi effect
62	US 2004026670 7 A1		US- PGPUB	20041230	159	Stabilized polynucleotides for use in RNA interference
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64	US 2004025924 8 A1		US- PGPUB	20041223	63	RNA interference mediating small RNA molecules
65	US 2004025924 7 A1		US- PGPUB	20041223	60	Rna interference mediating small rna molecules
66	US 2004022926 7 A1		US- PGPUB	20041118	86	Tumor suppressor pathway in C. elegans
67	US 2004022926 6 A1		US- PGPUB	20041118	60	RNA interference mediating small RNA molecules
68	US 2004022440 5 A1		US- PGPUB	20041111	57	siRNA induced systemic gene silencing in mammalian systems
69	US 2004019864 0 A1		US- PGPUB	20041007	66	Stabilized polynucleotides for use in RNA interference
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71	US 2004017628 2 A1		US- PGPUB	20040909	61	Cellular delivery and activation of polypeptide-nucleic acid complexes
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77	US 2004008691 1 A1		US- PGPUB	20040506	35	Inhibition of gene expression in vertebrates using double-stranded RNA (RNAi)
78	US 2004008688 4 A1		US- PGPUB	20040506	126	Methods and compositions for RNA interference
79	US 2004004504 3 A1		US- PGPUB	20040304	38	Compositions and methods for generating conditional knockouts

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86	US 2003014359 7 A1		US- PGPUB	20030731	40	Methods for making polynucleotide libraries, polynucleotide arrays, and cell libraries for high-throughput genomics analysis
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99	US 7078196 B2		USPAT	20060718	67	RNA interference mediating small RNA molecules
100	US 7056704 B2		USPAT	20060606	65	RNA interference mediating small RNA molecules
101	US 7001739 B2		USPAT	20060221	47	Isolation of proteins involved in posttranscriptional gene silencing and methods of use
102	US 6573099 B2		USPAT	20030603	46	Genetic constructs for delaying or repressing the expression of a target gene
103	US 6506559 B1		USPAT	20030114	24	Genetic inhibition by double-stranded RNA